STIC Search


```
=> fil jic pascal biotechno esbio biosis biotechds dissabs wpids; d que 161
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L48          2946 SEA SYNDECAN#
L49           908 SEA CD138 OR CD 138 OR SDC1 OR SDC 1 OR XSYN#
L50        596848 SEA FUSION OR FUSED OR CHIMER? OR CHIMAER?
L51        507547 SEA GROWTH FACTOR#
L52         42448 SEA GMCSF OR GRANULOCYTE MACROPHAGE COLONY STIMULATING FACTOR
L53        125106 SEA INTERFERON(A) GAMMA
L54         22185 SEA INTERLEUKIN 3
L55          2158 SEA PERMEABILITY FACTOR
L61            29 SEA (L48 OR L49) (S) L50 (S) (L51 OR L52 OR L53 OR L54 OR L55)


=> fil capl; d que l11; d que l18; d que l20
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FILE COVERS 1907 - 25 Mar 2005  VOL 142 ISS 14
FILE LAST UPDATED: 24 Mar 2005  (20050324/ED)
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Searched by Barb O'Bryen, STIC 2-2518

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

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L1            54 SEA FILE=REGISTRY ABB=ON  SYNDECAN?/CN
L2            54 SEA FILE=CAPLUS ABB=ON  L1
L4        186004 SEA FILE=CAPLUS ABB=ON  FUSION/OBI OR FUSED/OBI
L5         29241 SEA FILE=CAPLUS ABB=ON  CHIMER?/OBI
L8           815 SEA FILE=CAPLUS ABB=ON  SYNDECANS+OLD,NT/CT
L9         32068 SEA FILE=CAPLUS ABB=ON  (L4 OR L5) (L) PROTEIN#/OBI
L11            4 SEA FILE=CAPLUS ABB=ON  L9 (L) (L2 OR L8)
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L1            54 SEA FILE=REGISTRY ABB=ON  SYNDECAN?/CN
L2            54 SEA FILE=CAPLUS ABB=ON  L1
L4        186004 SEA FILE=CAPLUS ABB=ON  FUSION/OBI OR FUSED/OBI
L5         29241 SEA FILE=CAPLUS ABB=ON  CHIMER?/OBI
L8           815 SEA FILE=CAPLUS ABB=ON  SYNDECANS+OLD,NT/CT
L9         32068 SEA FILE=CAPLUS ABB=ON  (L4 OR L5) (L) PROTEIN#/OBI
L12       126234 SEA FILE=CAPLUS ABB=ON  GROWTH FACTOR#/OBI
L13        16824 SEA FILE=CAPLUS ABB=ON  GMCSF/OBI OR COLONY STIMULATING
                 FACTOR/OBI
L14          452 SEA FILE=CAPLUS ABB=ON  PERMEABILITY FACTOR/OBI
L15        15587 SEA FILE=CAPLUS ABB=ON  INTERFERON/OBI (L) GAMMA/OBI
L16         9065 SEA FILE=CAPLUS ABB=ON  INTERLEUKIN#/OBI (L) 3/OBI
L18            2 SEA FILE=CAPLUS ABB=ON  L9 AND (L2 OR L8) (L) (L12 OR L13 OR
                 L14 OR L15 OR L16)
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L1            54 SEA FILE=REGISTRY ABB=ON  SYNDECAN?/CN
L2            54 SEA FILE=CAPLUS ABB=ON  L1
L8           815 SEA FILE=CAPLUS ABB=ON  SYNDECANS+OLD,NT/CT
L12       126234 SEA FILE=CAPLUS ABB=ON  GROWTH FACTOR#/OBI
L13        16824 SEA FILE=CAPLUS ABB=ON  GMCSF/OBI OR COLONY STIMULATING
                 FACTOR/OBI
L14          452 SEA FILE=CAPLUS ABB=ON  PERMEABILITY FACTOR/OBI
L15        15587 SEA FILE=CAPLUS ABB=ON  INTERFERON/OBI (L) GAMMA/OBI
L16         9065 SEA FILE=CAPLUS ABB=ON  INTERLEUKIN#/OBI (L) 3/OBI
L19        18293 SEA FILE=CAPLUS ABB=ON  "FUSION PROTEINS (CHIMERIC PROTEINS)"+O
                 LD/CT
L20            5 SEA FILE=CAPLUS ABB=ON  L19 AND (L2 OR L8) AND (L12 OR L13 OR
                 L14 OR L15 OR L16)
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=> s l11 or l18 or l20
L63            7 L11 OR L18 OR L20

=> fil medl; d que l25; fil embase; d que l47
FILE 'MEDLINE' ENTERED AT 17:19:29 ON 25 MAR 2005

 FILE LAST UPDATED: 24 MAR 2005 (20050324/UP).  FILE COVERS 1950 TO DATE.

 On December 19, 2004, the 2005 MeSH terms were loaded.

 The MEDLINE reload for 2005 is now available.  For details enter HELP
```

RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L21          976 SEA FILE=MEDLINE ABB=ON  SYNDECAN#
L22        51911 SEA FILE=MEDLINE ABB=ON  RECOMBINANT FUSION PROTEINS+NT/CT
L24       418403 SEA FILE=MEDLINE ABB=ON  GROWTH SUBSTANCES+NT/CT
L25           14 SEA FILE=MEDLINE ABB=ON  L21 AND L22 AND L24
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FILE 'EMBASE' ENTERED AT 17:19:29 ON 25 MAR 2005

FILE COVERS 1974 TO 24 Mar 2005 (20050324/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L28          965 SEA FILE=EMBASE ABB=ON  SYNDECAN/CT OR  SYNDECAN 1/CT OR
                 SYNDECAN 2/CT OR SYNDECAN 3/CT OR SYNDECAN 4/CT
L29        16006 SEA FILE=EMBASE ABB=ON  HYBRID PROTEIN/CT
L30         3084 SEA FILE=EMBASE ABB=ON  CHIMERIC PROTEIN/CT
L32         6096 SEA FILE=EMBASE ABB=ON  FIBROBLAST GROWTH FACTOR/CT
L33         1225 SEA FILE=EMBASE ABB=ON  ACIDIC FIBROBLAST GROWTH FACTOR/CT
L34         7986 SEA FILE=EMBASE ABB=ON  BASIC FIBROBLAST GROWTH FACTOR/CT
L35            0 SEA FILE=EMBASE ABB=ON  KEPATINOCYTE GROWTH FACTOR
L36        15391 SEA FILE=EMBASE ABB=ON  GRANULOCYTE MACROPHAGE COLONY STIMULATI
                 NG FACTOR/CT
L37         3855 SEA FILE=EMBASE ABB=ON  SCATTER FACTOR/CT
L38         8476 SEA FILE=EMBASE ABB=ON  PLATELET DERIVED GROWTH FACTOR+NT/CT
L39        16020 SEA FILE=EMBASE ABB=ON  TRANSFORMING GROWTH FACTOR BETA+NT/CT
L40        13119 SEA FILE=EMBASE ABB=ON  VASCULOTROPIN/CT
L41        13119 SEA FILE=EMBASE ABB=ON  VASCULOTROPIN/CT
L42        46196 SEA FILE=EMBASE ABB=ON  GAMMA INTERFERON/CT
L43         7548 SEA FILE=EMBASE ABB=ON  INTERLEUKIN 3/CT
L44            2 SEA FILE=EMBASE ABB=ON  SCHWANNOMA DERIVED GROWTH FACTOR/CT
L45          981 SEA FILE=EMBASE ABB=ON  KERATINOCYTE GROWTH FACTOR/CT
L47            2 SEA FILE=EMBASE ABB=ON  L28 AND (L29 OR L30) AND (L32 OR L33
                 OR L34 OR L35 OR L36 OR L37 OR L38 OR L39 OR L40 OR L41 OR L42
                 OR L43 OR L44 OR L45)
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=> dup rem l25,l63,l61,l47
FILE 'MEDLINE' ENTERED AT 17:19:41 ON 25 MAR 2005

FILE 'CAPLUS' ENTERED AT 17:19:41 ON 25 MAR 2005
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FILE 'ESBIOBASE' ENTERED AT 17:19:41 ON 25 MAR 2005

FILE 'BIOSIS' ENTERED AT 17:19:41 ON 25 MAR 2005

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FILE 'WPIDS' ENTERED AT 17:19:41 ON 25 MAR 2005

FILE 'EMBASE' ENTERED AT 17:19:41 ON 25 MAR 2005

PROCESSING COMPLETED FOR L25
PROCESSING COMPLETED FOR L63
PROCESSING COMPLETED FOR L61
PROCESSING COMPLETED FOR L47
L64 33 DUP REM L25 L63 L61 L47 (19 DUPLICATES REMOVED)
ANSWERS '1-14' FROM FILE MEDLINE
ANSWERS '15-21' FROM FILE CAPLUS
ANSWERS '22-23' FROM FILE JICST-EPLUS
ANSWER '24' FROM FILE PASCAL
ANSWERS '25-28' FROM FILE BIOTECHNO
ANSWER '29' FROM FILE ESBIOBASE
ANSWERS '30-32' FROM FILE BIOTECHDS
ANSWER '33' FROM FILE WPIDS

=> d iall 1-14; d ibib ed abs hitind 15-21; d iall 22-33; fil hom

L64 ANSWER 1 OF 33 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2002291903 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11889131
TITLE: Clustering induces redistribution of **syndecan**-4 core protein into raft membrane domains.
COMMENT: Erratum in: J Biol Chem 2002 Sep 20;277(38):35778
AUTHOR: Tkachenko Eugene; Simons Michael
CORPORATE SOURCE: Angiogenesis Research Center and Section of Cardiology, Department of Medicine, Dartmouth Medical School, Lebanon, New Hampshire 03756, USA.
SOURCE: Journal of biological chemistry, (2002 May 31) 277 (22) 19946-51. Electronic Publication: 2002-03-11. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 20020529
Last Updated on STN: 20030105
Entered Medline: 20020702

ABSTRACT:
Syndecan-4 is a heparan sulfate-carrying core protein that has been directly implicated in fibroblast growth factor 2 (FGF2) signaling. Recent studies have suggested that many signaling proteins localize to the raft compartment of the plasma cell membrane. To establish whether **syndecan**-4 is present in the raft compartment, we have studied the distribution of the core protein and an Fc receptor (FcR)-**syndecan**-4 chimera prior to and following clustering with FGF2 or antibodies. Whereas unclustered ***syndecan*** -4 was present predominantly in the non-raft membrane compartment, clustering induced extensive **syndecan**-4 redistribution to the rafts as demonstrated by the sucrose gradient centrifugation and life confocal microscopy. Although **syndecan**-4 and caveolin-1 moved in tandem, **syndecan**-4 was not present in caveolae, a major subset of raft compartments. We conclude that **syndecan**-4 clustering induces its redistribution to the non-caveolae raft compartment. This process may play an important role in **syndecan**-4-mediation of FGF2 signaling.

CONTROLLED TERM:
Animals
Biotinylation
Caveolins: CH, chemistry
Caveolins: ME, metabolism
Cell Line
Cell Separation
Cells, Cultured
DNA, Complementary: ME, metabolism
Fibroblast Growth Factor 2: ME, metabolism
Flow Cytometry
Humans
Immunoblotting
*Membrane Glycoproteins: CH, chemistry
*Membrane Microdomains: CH, chemistry
*Membrane Microdomains: ME, metabolism
Microscopy, Confocal
Microscopy, Fluorescence
Precipitin Tests
Protein Binding
*Proteoglycans: CH, chemistry
Rats
Recombinant Fusion Proteins: ME, metabolism
Signal Transduction
Sucrose: ME, metabolism
Transfection

CAS REGISTRY NO.: 103107-01-3 (Fibroblast Growth Factor 2); 149720-12-7 (caveolin 1); 57-50-1 (Sucrose)
CHEMICAL NAME: 0 (Caveolins); 0 (DNA, Complementary); 0 (Membrane Glycoproteins); 0 (Proteoglycans); 0 (Recombinant Fusion Proteins); 0 (**syndecan**-4)

L64 ANSWER 2 OF 33 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 1999042003 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9822708
TITLE: **Syndecan**-1 expression inhibits myoblast differentiation through a basic fibroblast growth factor-dependent mechanism.

AUTHOR: Larrain J; Carey D J; Brandan E
CORPORATE SOURCE: Department of Cell and Molecular Biology, Faculty of Biological Sciences, Catholic University of Chile, Santiago, Chile.
CONTRACT NUMBER: NS21925 (NINDS)
TW 00093 (FIC)
SOURCE: Journal of biological chemistry, (1998 Nov 27) 273 (48) 32288-96.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981223

ABSTRACT:
Expression of **syndecan**-1, a cell-surface heparan sulfate proteoglycan, is down-regulated during skeletal muscle differentiation (Larrain, J., Cizmeci-Smith, G., Troncoso, V., Stahl, R. C., Carey, D. J., and Brandan, E. (1997) J. Biol. Chemical 272, 18418-18424). We examined the role of **syndecan**-1 in basic fibroblast growth factor (bFGF)-dependent inhibition of myogenesis. C2C12 myoblasts were stably transfected with an expression plasmid containing the rat **syndecan**-1 coding region cDNA. Constitutive **syndecan**-1 expression resulted in a strongly diminished capacity of the transfected clones to differentiate and to express skeletal muscle-specific markers such as fusion, creatine kinase, and myosin. The expression of myogenin, a master transcription factor for muscle differentiation, was also reduced and delayed. Analysis of the induction of a myogenin promoter-driven reporter revealed that **syndecan**-1 expression resulted in a 6-7-fold increase in sensitivity to bFGF-dependent inhibition of myogenin expression. Transfecting the cells with a plasmid containing myogenin cDNA reversed the inhibition of myogenin transcriptional activation and myosin expression in **syndecan**-1-transfected cells; however, cell fusion was not observed. These results demonstrate that **syndecan**-1 expression enhances cell responsiveness to bFGF and inhibits myoblast fusion and suggest that muscle terminal differentiation is regulated by **syndecan**-1 expression.

CONTROLLED TERM:
Animals
Biological Markers
Cell Differentiation: DE, drug effects
Cell Differentiation: PH, physiology
Cell Fusion
Cell Line
Chloramphenicol O-Acetyltransferase: BI, biosynthesis
Creatine Kinase: GE, genetics
Fibroblast Growth Factor 2: PD, pharmacology
***Fibroblast Growth Factor 2: PH, physiology**
Genes, Reporter
Genomic Library
Heparin: PD, pharmacology
Kinetics
Membrane Glycoproteins: GE, genetics
*Membrane Glycoproteins: PH, physiology
Mice
Mice, Inbred BALB C
*Muscle, Skeletal: CY, cytology
Muscle, Skeletal: DE, drug effects
*Muscle, Skeletal: ME, metabolism

Myogenin: BI, biosynthesis
Myogenin: GE, genetics
Myosin Heavy Chains: AN, analysis
Myosin Heavy Chains: GE, genetics
Proteoglycans: GE, genetics
*Proteoglycans: PH, physiology
Rats
*Receptor Protein-Tyrosine Kinases
Receptors, Fibroblast Growth Factor: AN, analysis
Receptors, Fibroblast Growth Factor: GE, genetics
Recombinant Fusion Proteins: BI, biosynthesis
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Time Factors
Transfection

CAS REGISTRY NO.: 103107-01-3 (Fibroblast Growth Factor 2); 9005-49-6 (Heparin)

CHEMICAL NAME: 0 (Biological Markers); 0 (Membrane Glycoproteins); 0 (Myogenin); 0 (Myosin Heavy Chains); 0 (Proteoglycans); 0 (Receptors, Fibroblast Growth Factor); 0 (Recombinant Fusion Proteins); 0 (**syndecan**); EC 2.3.1.28 (Chloramphenicol O-Acetyltransferase); EC 2.7.1.112 (Receptor Protein-Tyrosine Kinases); EC 2.7.1.112 (fibroblast growth factor receptor 1); EC 2.7.3.2 (Creatine Kinase)

L64 ANSWER 3 OF 33 MEDLINE on STN
ACCESSION NUMBER: 2004467451 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15280392
TITLE: Angiopoietin-3 is tethered on the cell surface via heparan sulfate proteoglycans.
AUTHOR: Xu Yin; Liu Yao-Juan; Yu Qin
CORPORATE SOURCE: Department of Pathobiology, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, Pennsylvania 19104, USA.
CONTRACT NUMBER: 5R01HL074117 (NHLBI)
SOURCE: Journal of biological chemistry, (2004 Sep 24) 279 (39) 41179-88. Electronic Publication: 2004-07-27.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 20040921
Last Updated on STN: 20041027
Entered Medline: 20041026

ABSTRACT:
Angiopoietins are a family of factors that play important roles in angiogenesis, and their receptor, Tie-2 receptor tyrosine kinase, is expressed primarily by endothelial cells. Three angiopoietins have been identified so far, angiopoietin-1 (Ang-1), angiopietin-2 (Ang-2), and angiopoietin-3 (Ang-3). It has been established that Ang-1 and Tie-2 play essential roles in embryonic angiogenesis. We have demonstrated recently that, unlike Ang-2, Ang-1 binds to the extracellular matrix, which regulates the availability and activity of Ang-1 (Xu, Y., and Yu, Q. (2001) J. Biol. Chemical 276, 34990-34998). However, the role and biochemical characteristics of Ang-3 are unknown. In our current study, we demonstrated that, unlike Ang-1 and Ang-2, Ang-3 is tethered on cell surface via heparan sulfate proteoglycans (HSPGs), especially perlecan. The cell surface-bound Ang-3 is capable of binding to its receptor, Tie-2;

suggesting HSPGs concentrate Ang-3 on the cell surface and present Ang-3 to its receptor to elicit specific local reaction. Mutagenesis experiment revealed that the coiled-coil domain of Ang-3 is responsible for its binding to the cell surface. In addition, we demonstrated that the cell surface-bound Ang-3 but not soluble Ang-3 induces retraction and loss of integrity of endothelial monolayer, indicating the binding of Ang-3 to the cell surface via HSPGs is required for this bioactivity of Ang-3.

CONTROLLED TERM: **Angiopoietin-1: ME, metabolism**
Angiopoietin-2: ME, metabolism
Angiopoietins: ME, metabolism
Animals
Blotting, Western
COS Cells
Cattle
Cell Line, Tumor
*Cell Membrane: ME, metabolism
Coculture Techniques
Endothelium, Vascular: ME, metabolism
Enzyme-Linked Immunosorbent Assay
Epitopes
Extracellular Matrix: ME, metabolism
Gene Deletion
*Heparan Sulfate Proteoglycan: CH, chemistry
Heparan Sulfate Proteoglycan: ME, metabolism
Heparitin Sulfate: CH, chemistry
Immunohistochemistry
***Intercellular Signaling Peptides and Proteins: PH, physiology**
Ligands
Membrane Glycoproteins: ME, metabolism
Mice
Muscle, Smooth: ME, metabolism
Mutagenesis
Protein Binding
Protein Structure, Tertiary
Proteoglycans: ME, metabolism
Receptor, TIE-2: ME, metabolism
Recombinant Fusion Proteins: ME, metabolism
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Reverse Transcriptase Polymerase Chain Reaction
Transfection

CAS REGISTRY NO.: 9050-30-0 (Heparitin Sulfate)

CHEMICAL NAME: 0 (ANGPTL1 protein, human); 0 (Angiopoietin-1); 0 (Angiopoietin-2); 0 (Angiopoietins); 0 (Epitopes); 0 (Heparan Sulfate Proteoglycan); 0 (Intercellular Signaling Peptides and Proteins); 0 (Ligands); 0 (Membrane Glycoproteins); 0 (Proteoglycans); 0 (Recombinant Fusion Proteins); 0 (**syndecan**); EC 2.7.1.112 (Receptor, TIE-2)

L64 ANSWER 4 OF 33 MEDLINE on STN

ACCESSION NUMBER: 2004324319 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15226395

TITLE: Fibroblast growth factor 2 endocytosis in endothelial cells proceed via **syndecan**-4-dependent activation of Rac1 and a Cdc42-dependent macropinocytic pathway.

AUTHOR: Tkachenko Eugene; Lutgens Esther; Stan Radu-Virgil; Simons Michael

CORPORATE SOURCE: Angiogenesis Research Center, Department of Medicine, Dartmouth Medical School, One Medical Center Drive, Lebanon, NH 03756, USA.
CONTRACT NUMBER: HL53793 (NHLBI)
HL62289 (NHLBI)
HL63609 (NHLBI)
HL65418 (NHLBI)
SOURCE: Journal of cell science, (2004 Jul 1) 117 (Pt 15) 3189-99.
Journal code: 0052457. ISSN: 0021-9533.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 20040701
Last Updated on STN: 20050208
Entered Medline: 20050207

ABSTRACT:
Full activity of fibroblast growth factors (FGFs) requires their internalization in addition to the interaction with cell surface receptors. Recent studies have suggested that the transmembrane proteoglycan ***syndecan*** -4 functions as a FGF2 receptor. In this study we investigated the molecular basis of **syndecan** endocytosis and its role in FGF2 internalization in endothelial cells. We found that **syndecan**-4 uptake, induced either by treatment with FGF2 or by antibody clustering, requires the integrity of plasma membrane lipid rafts for its initiation, occurs in a non-clathrin-, non-dynamin-dependent manner and involves Rac1, which is activated by **syndecan**-4 clustering. FGF2 was internalized in a complex with **syndecan**-4 in 70 kDa dextran-containing endocytic vesicles. FGF2 and **syndecan**-4 but not dextran endocytosis were blocked by the dominant negative Rac1 while amiloride and the dominant-negative Cdc42 blocked internalization of dextran in addition to FGF2 and ***syndecan*** -4. Taken together, these results demonstrate that FGF2 endocytosis requires **syndecan**-4 clustering-dependent activation of Rac1 and the intact CDC42-dependent macropinocytic pathway.

CONTROLLED TERM:
Animals
Cell Line
Cell Membrane: ME, metabolism
Cells, Cultured
Cholesterol: ME, metabolism
DNA, Complementary: ME, metabolism
Dextrans: ME, metabolism
*Endocytosis
*Endothelium, Vascular: ME, metabolism
Enzyme Activation
Fibroblast Growth Factor 2: ME, metabolism
***Fibroblast Growth Factor 2: PH, physiology**
Fluorescent Dyes: PD, pharmacology
GTP Phosphohydrolases: ME, metabolism
Growth Substances: ME, metabolism
Heparitin Sulfate: ME, metabolism
Membrane Glycoproteins: GE, genetics
*Membrane Glycoproteins: ME, metabolism
Membrane Microdomains: ME, metabolism
Microscopy, Fluorescence
Multigene Family
Pinocytosis
Protein Binding
Proteoglycans: GE, genetics
*Proteoglycans: ME, metabolism

Rats
Recombinant Fusion Proteins: ME, metabolism
Research Support, U.S. Gov't, P.H.S.
Signal Transduction
Time Factors
Transfection
*cdc42 GTP-Binding Protein: ME, metabolism
rac1 GTP-Binding Protein: ME, metabolism
*rac1 GTP-Binding Protein: PH, physiology

CAS REGISTRY NO.: 103107-01-3 (Fibroblast Growth Factor 2); 57-88-5 (Cholesterol); 9004-54-0 (Dextrans); 9050-30-0 (Heparitin Sulfate)

CHEMICAL NAME: 0 (DNA, Complementary); 0 (Fluorescent Dyes); 0 (Growth Substances); 0 (Membrane Glycoproteins); 0 (Proteoglycans); 0 (Recombinant Fusion Proteins); 0 (**syndecan**); 0 (**syndecan**-4); EC 3.6.1.- (GTP Phosphohydrolases); EC 3.6.1.- (cdc42 GTP-Binding Protein); EC 3.6.1.- (rac1 GTP-Binding Protein)

L64 ANSWER 5 OF 33 MEDLINE on STN
ACCESSION NUMBER: 2002000517 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11585825
TITLE: **Syndecan**-4 deficiency leads to high mortality of lipopolysaccharide-injected mice.
AUTHOR: Ishiguro K; Kadomatsu K; Kojima T; Muramatsu H; Iwase M; Yoshikai Y; Yanada M; Yamamoto K; Matsushita T; Nishimura M; Kusugami K; Saito H; Muramatsu T
CORPORATE SOURCE: Department of Biochemistry, Nagoya University School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya, Aichi, 466-8550, Japan.
SOURCE: Journal of biological chemistry, (2001 Dec 14) 276 (50) 47483-8. Electronic Publication: 2001-10-03. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20020102
Last Updated on STN: 20030105
Entered Medline: 20020124

ABSTRACT:
Syndecan-4 is a transmembrane heparan sulfate proteoglycan belonging to the **syndecan** family. Following intraperitoneal injection of lipopolysaccharide (LPS), **syndecan**-4-deficient mice exhibited high mortality compared with wild-type controls. Severe endotoxin shock was observed in the deficient mice: systolic blood pressure and left ventricular fractional shortening were lower in the deficient mice than in the wild-type controls 9 h after LPS injection. Although histological examinations revealed no apparent differences between two groups, the plasma level of interleukin (IL)-1beta was higher in the deficient mice than in the wild-type controls 9 h after LPS injection. Consistent with the regulatory roles of **syndecan**-4, its expression in monocytes and endothelial cells of microvasculature increased in the wild-type mice after LPS administration. Although IL-1beta was produced to the same extent by macrophages from **syndecan**-4-deficient and wild-type mice after LPS stimulation, inhibition of its production by transforming growth factor-beta1 was impaired in the ***syndecan*** -4-deficient macrophages. These results indicate that ***syndecan*** -4 could be involved in prevention of endotoxin shock, at least partly through the inhibitory action of transforming growth factor-beta1 on

IL-1beta production.
CONTROLLED TERM: Animals
Blood Pressure: DE, drug effects
Cytokines: BL, blood
Endothelium: ME, metabolism
Flow Cytometry
Glutathione Transferase: ME, metabolism
Immunohistochemistry
Injections, Intraperitoneal
Interleukin-1: BL, blood
Interleukin-10: BI, biosynthesis
*Lipopolysaccharides: PD, pharmacology
Liver: ME, metabolism
Macrophages: ME, metabolism
*Membrane Glycoproteins: DF, deficiency
Mice
Mice, Inbred C57BL
Monocytes: ME, metabolism
Protein Binding
*Proteoglycans: DF, deficiency
Recombinant Fusion Proteins: ME, metabolism
Research Support, Non-U.S. Gov't
*Shock: MO, mortality
Time Factors
Transforming Growth Factor beta: ME, metabolism
Ventricular Function, Left: DE, drug effects
CAS REGISTRY NO.: 130068-27-8 (Interleukin-10)
CHEMICAL NAME: 0 (Cytokines); 0 (Interleukin-1); 0 (Lipopolysaccharides); 0 (Membrane Glycoproteins); 0 (Proteoglycans); 0 (Recombinant Fusion Proteins); 0 (Transforming Growth Factor beta); 0 (**syndecan**-4); EC 2.5.1.18 (Glutathione Transferase)

L64 ANSWER 6 OF 33 MEDLINE on STN
ACCESSION NUMBER: 2001678852 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11724824
TITLE: Role of heparan sulfate as a tissue-specific regulator of FGF-4 and FGF receptor recognition.
AUTHOR: Allen B L; Filla M S; Rapraeger A C
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, University of Wisconsin-Madison, Madison, WI 53706, USA.
CONTRACT NUMBER: R01-GM48850 (NIGMS)
SOURCE: Journal of cell biology, (2001 Nov 26) 155 (5) 845-58. Electronic Publication: 2001-11-26. Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011129
Last Updated on STN: 20030105
Entered Medline: 20020108

ABSTRACT:
FGF signaling uses receptor tyrosine kinases that form high-affinity complexes with FGFs and heparan sulfate (HS) proteoglycans at the cell surface. It is hypothesized that assembly of these complexes requires simultaneous recognition of distinct sulfation patterns within the HS chain by FGF and the FGF receptor (FR), suggesting that tissue-specific HS synthesis may regulate FGF signaling. To address this, FGF-2 and FGF-4, and extracellular domain constructs of

FR1-IIIc (FR1c) and FR2-IIIc (FR2c), were used to probe for tissue-specific HS in embryonic day 18 mouse embryos. Whereas FGF-2 binds HS ubiquitously, FGF-4 exhibits a restricted pattern, failing to bind HS in the heart and blood vessels and failing to activate signaling in mouse aortic endothelial cells. This suggests that FGF-4 seeks a specific HS sulfation pattern, distinct from that of FGF-2, which is not expressed in most vascular tissues. Additionally, whereas FR2c binds all FGF-4-HS complexes, FR1c fails to bind FGF-4-HS in most tissues, as well as in Raji-S1 cells expressing **syndecan**-1. Proliferation assays using BaF3 cells expressing either FR1c or FR2c support these results. This suggests that FGF and FR recognition of specific HS sulfation patterns is critical for the activation of FGF signaling, and that synthesis of these patterns is regulated during embryonic development.

CONTROLLED TERM:
Animals
Brain: BS, blood supply
Brain: EM, embryology
Cells, Cultured
Embryo: ME, metabolism
Endothelium, Vascular: CY, cytology
Endothelium, Vascular: ME, metabolism
Fibroblast Growth Factor 2: CH, chemistry
Fibroblast Growth Factor 2: ME, metabolism
***Fibroblast Growth Factors: ME, metabolism**
Heparin: PD, pharmacology
Heparitin Sulfate: CH, chemistry
*Heparitin Sulfate: ME, metabolism
Immunohistochemistry
Isoenzymes: GE, genetics
Isoenzymes: ME, metabolism
Kidney: CY, cytology
Kidney: EM, embryology
Kidney: ME, metabolism
Liver: CY, cytology
Liver: EM, embryology
Liver: ME, metabolism
Lung: CY, cytology
Lung: EM, embryology
Lung: ME, metabolism
Mice
Molecular Structure
Myocardium: CH, chemistry
Myocardium: ME, metabolism
Protein Binding
*Proto-Oncogene Proteins: ME, metabolism
Receptor Protein-Tyrosine Kinases: ME, metabolism
*Receptors, Fibroblast Growth Factor: ME, metabolism
Recombinant Fusion Proteins: ME, metabolism
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Signal Transduction: PH, physiology
Skin: CH, chemistry
Skin: CY, cytology
Skin: EM, embryology

CAS REGISTRY NO.: 103107-01-3 (Fibroblast Growth Factor 2); 62031-54-3 (Fibroblast Growth Factors); 9005-49-6 (Heparin); 9050-30-0 (Heparitin Sulfate)

CHEMICAL NAME: 0 (Isoenzymes); 0 (Proto-Oncogene Proteins); 0 (Receptors, Fibroblast Growth Factor); 0 (Recombinant Fusion Proteins); 0 (carcinoplacental isoenzymes); 0 (fibroblast growth factor 4); EC 2.7.1.112 (Receptor Protein-Tyrosine Kinases); EC 2.7.1.112 (fibroblast growth factor receptor

1); EC 2.7.1.112 (fibroblast growth factor receptor 2)

L64 ANSWER 7 OF 33 MEDLINE on STN
ACCESSION NUMBER: 2000387138 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10770943
TITLE: Syntenin-**syndecan** binding requires **syndecan**-synteny and the co-operation of both PDZ domains of syntenin.
AUTHOR: Grootjans J J; Reekmans G; Ceulemans H; David G
CORPORATE SOURCE: Laboratory for Glycobiology and Developmental Genetics, Center for Human Genetics, University of Leuven, B-3000 Leuven, Belgium.
SOURCE: Journal of biological chemistry, (2000 Jun 30) 275 (26) 19933-41.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000818
Last Updated on STN: 20000818
Entered Medline: 20000810

ABSTRACT:
Syntenin is an adaptor-like molecule that binds to the cytoplasmic domains of all four vertebrate **syndecans.** Syntenin-**syndecan** binding involves the C-terminal part of syntenin that contains a tandem of PDZ domains. Here we provide evidence that each PDZ domain of syntenin can interact with a ***syndecan.*** Isolated or combined mutations of the carboxylate binding lysines in the inter-betaAbetaB loops and of the alphaB1 residues in either one or both the PDZ domains of syntenin all reduce syntenin-**syndecan** binding in yeast two-hybrid, blot-overlay, and surface plasmon resonance assays. PDZ2 mutations have more pronounced effects on binding than PDZ1 mutations, but complete abrogation of syntenin-**syndecan** binding requires the combination of both the lysine and the alphaB1 mutations in both the PDZ domains of syntenin. Isothermal calorimetric titration of syntenin with **syndecan** peptide reveals the presence of two binding sites in syntenin. Yet, unlike a tandem of two PDZ2 domains and a reconstituted PDZ1+PDZ2 tandem, a tandem of two PDZ1 domains and isolated PDZ1 or PDZ2 domains do not interact with **syndecan** bait. We conclude to a co-operative binding mode whereby neither of these two PDZ domains is sufficient by itself but where PDZ2 functions as a "major" or "high affinity" ***syndecan*** binding domain, and PDZ1 functions as an "accessory" or "low affinity" **syndecan** binding domain. The paired, but not the isolated PDZ domains of syntenin bind also strongly to the immobilized cytoplasmic domains of neurexin and B-class ephrins. By inference, these data suggest a model whereby recruitment of syntenin to membrane surfaces requires two compatible types of bait that are in "synteny" (occurring together in location) and engages both PDZ domains of syntenin. The synteny of compatible bait may result from the assemblies and co-assemblies of **syndecans** and other similarly suited partners in larger supramolecular complexes. In general, an intramolecular combination of PDZ domains that are weak, taken individually, would appear to be designed to detect rather than drive the formation of specific molecular assemblies.

CONTROLLED TERM: Amino Acid Sequence
Calorimetry
*Carrier Proteins: CH, chemistry
Carrier Proteins: GE, genetics
*Carrier Proteins: ME, metabolism
Cytoplasm: ME, metabolism

DNA, Complementary: ME, metabolism
Ephrin-B1
Escherichia coli: ME, metabolism
Glutathione Transferase: ME, metabolism
Humans
*Intracellular Signaling Peptides and Proteins
Ligands
*Membrane Glycoproteins: CH, chemistry
Membrane Glycoproteins: GE, genetics
*Membrane Glycoproteins: ME, metabolism
Membrane Proteins: ME, metabolism
Molecular Sequence Data
Mutagenesis, Site-Directed
Nerve Tissue Proteins: ME, metabolism
Peptides: ME, metabolism
Point Mutation
Protein Binding
Protein Structure, Secondary
Protein Structure, Tertiary
*Proteoglycans: CH, chemistry
Proteoglycans: GE, genetics
*Proteoglycans: ME, metabolism
Recombinant Fusion Proteins: ME, metabolism
Research Support, Non-U.S. Gov't
Sequence Homology, Amino Acid
Surface Plasmon Resonance
Time Factors
Two-Hybrid System Techniques

CHEMICAL NAME: 0 (Carrier Proteins); 0 (DNA, Complementary); 0 (Ephrin-B1); 0 (Intracellular Signaling Peptides and Proteins); 0 (Ligands); 0 (Membrane Glycoproteins); 0 (Membrane Proteins); 0 (Nerve Tissue Proteins); 0 (Peptides); 0 (Proteoglycans); 0 (Recombinant Fusion Proteins); 0 (SDCBP protein, human); 0 (neurexin II); 0 (**syndecan**); EC 2.5.1.18 (Glutathione Transferase)

L64 ANSWER 8 OF 33 MEDLINE on STN
ACCESSION NUMBER: 2000472146 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10964499
TITLE: **Syndecan**-1 signals independently of beta1 integrins during Raji cell spreading.
AUTHOR: Lebakken C S; McQuade K J; Rapraeger A C
CORPORATE SOURCE: Program in Cellular and Molecular Biology, University of Wisconsin-Madison, Madison, Wisconsin, 53706, USA.. acraprae@facstaff.wisc.edu
CONTRACT NUMBER: HD21881 (NICHD)
T32-GM08349 (NIGMS)
SOURCE: Experimental cell research, (2000 Sep 15) 259 (2) 315-25. Journal code: 0373226. ISSN: 0014-4827.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20001012
Last Updated on STN: 20001012
Entered Medline: 20000929

ABSTRACT:
Syndecan-1-expressing Raji lymphoid cells (Raji-S1 cells) bind and spread rapidly when attaching to matrix ligands that contain heparan

sulfate-binding domains. However, these ligands also contain binding sites for integrins, which are widely known to signal, raising the question of whether the proteoglycan core protein participates in generation of the signal for spreading. To address this question, the spreading of the Raji-S1 cells is examined on ligands specific for either beta1 integrins, known to be present on the Raji cells, or the **syndecan**-1 core protein. The cells adhere and spread on invasin, a ligand that activates beta1 integrins, the IIICS fragment of fibronectin, which is a specific ligand for the alpha4beta1 integrin, or mAb281.2, an antibody specific for the **syndecan**-1 core protein. The signaling resulting from adhesion to the **syndecan**-specific antibody appears integrin independent as (i) the morphology of the cells spreading on the antibody is distinct from spreading initiated by the integrins alone; (ii) spreading on the **syndecan** or integrin ligands is affected differently by the kinase inhibitors tyrphostin 25, genistein, and staurosporine; and (iii) spreading on the **syndecan**-specific antibody is not disrupted by blocking beta1 integrin activation with mAb13, a beta1 inhibitory antibody. These data demonstrate that ligation of **syndecan**-1 initiates intracellular signaling and suggest that this signaling occurs when cells expressing **syndecan**-1 adhere to matrix ligands containing heparan sulfate-binding domains.

CONTROLLED TERM:
Antibodies, Monoclonal: PD, pharmacology
Antigens, CD29: IM, immunology
*Antigens, CD29: ME, metabolism
*B-Lymphocytes: CY, cytology
B-Lymphocytes: PH, physiology
Cell Adhesion: DE, drug effects
Cell Adhesion: PH, physiology
Cell Size: DE, drug effects
Cell Size: PH, physiology
Chimeric Proteins: GE, genetics
Chimeric Proteins: ME, metabolism
Enzyme Inhibitors: PD, pharmacology
Extracellular Matrix Proteins: PH, physiology
Genistein: PD, pharmacology
Heparan Sulfate Proteoglycan: PH, physiology
Humans
Lymphoma, B-Cell
Membrane Glycoproteins: GE, genetics
Membrane Glycoproteins: IM, immunology
*Membrane Glycoproteins: ME, metabolism
Neutralization Tests
Peptide Fragments: GE, genetics
Peptide Fragments: ME, metabolism
Proteoglycans: GE, genetics
Proteoglycans: IM, immunology
*Proteoglycans: ME, metabolism
Research Support, U.S. Gov't, P.H.S.
*Signal Transduction: PH, physiology
Staurosporine: PD, pharmacology
Tumor Cells, Cultured
Tyrphostins: PD, pharmacology

CAS REGISTRY NO.: 118409-58-8 (tyrphostin 25); 446-72-0 (Genistein); 62996-74-1 (Staurosporine)

CHEMICAL NAME: 0 (Antibodies, Monoclonal); 0 (Antigens, CD29); 0 (Chimeric Proteins); 0 (Enzyme Inhibitors); 0 (Extracellular Matrix Proteins); 0 (Heparan Sulfate Proteoglycan); 0 (Membrane Glycoproteins); 0 (Peptide Fragments); 0 (Proteoglycans); 0 (Tyrphostins); 0 (**syndecan**)

L64 ANSWER 9 OF 33 MEDLINE on STN
ACCESSION NUMBER: 2001019342 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10830734
TITLE: **Syndecans** and the lymphoid system.
AUTHOR: Kopper L; Sebestyen A
CORPORATE SOURCE: 1st Institute of Pathology and Experimental Cancer Research, Semmelweis University of Medicine, Budapest, Hungary.. kopper@korb1.sote.hu
SOURCE: Leukemia & lymphoma, (2000 Jul) 38 (3-4) 271-81. Ref: 88
Journal code: 9007422. ISSN: 1042-8194.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001103

ABSTRACT:
Syndecans, transmembrane proteoglycans, play an important role in cell-matrix and cell-cell interactions, as well as modulators in receptor activation. These functions are partly non-specific and related to the heparan sulfate chains attached to the ectodomain, and partly specific due to the transmembrane and cytoplasmic domains of the core protein. In hemopoietic cells **syndecan**-1 is expressed only in B cells at certain differentiation stages (pre-B and plasma cells). In lymphoproliferative conditions this selective expression is retained in myelomas/plasmacytomas and other lymphoplasmacytic NHL subtypes, and primary effusional lymphomas. It is probably gained in B-CLL, and lost in other NHLs of pre- or post-follicular origin. It is concluded from these empiric results that the expression of ***syndecan*** is essential for some NHLs, probably ensuring the required connections to the microenvironment. From a diagnostic point of view, ***syndecan*** -1 is a very useful phenotypic marker to indentify cells with plasmacytic differentiation. The importance of **syndecan** expression in CLL and Hodgkin's lymphoma still requires further studies.

CONTROLLED TERM:
Animals
B-Lymphocytes: CY, cytology
B-Lymphocytes: ME, metabolism
Cell Adhesion: PH, physiology
Cell Communication: PH, physiology
Cell Differentiation
Chromosomes, Human, Pair 2: GE, genetics
Cytokines: ME, metabolism
Extracellular Matrix: PH, physiology
Gene Expression Regulation
Humans
Interleukin-6: PD, pharmacology
*Lymphoid Tissue: ME, metabolism
Lymphoma: ME, metabolism
Lymphoma: PA, pathology
Lymphoproliferative Disorders: ME, metabolism
Lymphoproliferative Disorders: PA, pathology
Macromolecular Substances
Membrane Glycoproteins: CH, chemistry
Membrane Glycoproteins: GE, genetics
*Membrane Glycoproteins: PH, physiology
Membrane Proteins: ME, metabolism
Metalloendopeptidases: ME, metabolism

Neoplasm Invasiveness
Neoplasm Proteins: PH, physiology
Plasmacytoma: ME, metabolism
Plasmacytoma: PA, pathology
Protein Conformation
Proteoglycans: CH, chemistry
Proteoglycans: GE, genetics
*Proteoglycans: PH, physiology
Receptors, Cytokine: ME, metabolism
Recombinant Fusion Proteins: PH, physiology
Research Support, Non-U.S. Gov't
Signal Transduction
Transfection
Tumor Markers, Biological

CHEMICAL NAME: 0 (Cytokines); 0 (Interleukin-6); 0 (Macromolecular Substances); 0 (Membrane Glycoproteins); 0 (Membrane Proteins); 0 (Neoplasm Proteins); 0 (Proteoglycans); 0 (Receptors, Cytokine); 0 (Recombinant Fusion Proteins); 0 (Tumor Markers, Biological); 0 (**syndecan**); EC 3.4.24 (Metalloendopeptidases); EC 3.4.24.- (ADAM 12 protein)

L64 ANSWER 10 OF 33 MEDLINE on STN
ACCESSION NUMBER: 97364775 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9218485
TITLE: **Syndecan**-1 expression is down-regulated during myoblast terminal differentiation. Modulation by growth factors and retinoic acid.
AUTHOR: Larrain J; Cizmeci-Smith G; Troncoso V; Stahl R C; Carey D J; Brandan E
CORPORATE SOURCE: Department of Cell and Molecular Biology, Faculty of Biological Sciences, Catholic University of Chile, Casilla 114-D, Santiago, Chile.
CONTRACT NUMBER: TW 00093 (FIC)
SOURCE: Journal of biological chemistry, (1997 Jul 18) 272 (29) 18418-24.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199708
ENTRY DATE: Entered STN: 19970902
Last Updated on STN: 19980206
Entered Medline: 19970818

ABSTRACT:
Syndecan-1 is an integral membrane proteoglycan involved in the interaction of cells with extracellular matrix proteins and growth factors. It is transiently expressed in several condensing mesenchymal tissues after epithelial induction. In this study we evaluated the expression of ***syndecan*** -1 during skeletal muscle differentiation. The expression of ***syndecan*** -1 as determined by Northern blot analyses and immunofluorescence microscopy is down-regulated during differentiation. The transcriptional activity of a **syndecan**-1 promoter construct is also down-regulated in differentiating muscle cells. The decrease in ***syndecan*** -1 gene expression is not dependent on the presence of E-boxes, binding sites for the MyoD family of transcription factors in the promoter region, or myogenin expression. Deletion of the region containing the E-boxes or treatment of differentiating cells with sodium butyrate, an inhibitor of myogenin expression, had no effect on **syndecan**-1 expression. Basic

fibroblast growth factor and transforming growth factor type beta, which are inhibitors of myogenesis, had little effect on **syndecan**-1 expression. When added together, however, they induced **syndecan**-1 expression. Retinoic acid, an inducer of myogenesis, inhibited **syndecan**-1 expression and abolished the effect of the growth factors. These results indicate that **syndecan**-1 expression is down-regulated during myogenesis and that growth factors and retinoic acid modulate **syndecan** -1 expression by a mechanism that is independent of myogenin.

CONTROLLED TERM: Animals
Cell Differentiation: DE, drug effects
*Cell Differentiation: PH, physiology
Cell Line
Chloramphenicol O-Acetyltransferase: BI, biosynthesis
Fibroblast Growth Factor 2: PD, pharmacology
*Gene Expression Regulation
Gene Expression Regulation: DE, drug effects
***Growth Substances: PD, pharmacology**
*Membrane Glycoproteins: BI, biosynthesis
Mice
Muscle, Skeletal: CY, cytology
Muscle, Skeletal: DE, drug effects
*Muscle, Skeletal: ME, metabolism
Myogenin: BI, biosynthesis
*Proteoglycans: BI, biosynthesis
Recombinant Fusion Proteins: BI, biosynthesis
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Transfection
Transforming Growth Factor beta: PD, pharmacology
*Tretinoin: PD, pharmacology

CAS REGISTRY NO.: 103107-01-3 (Fibroblast Growth Factor 2); 302-79-4 (Tretinoin)

CHEMICAL NAME: 0 (Growth Substances); 0 (Membrane Glycoproteins); 0 (Myogenin); 0 (Proteoglycans); 0 (Recombinant Fusion Proteins); 0 (Transforming Growth Factor beta); 0 (**syndecan**); EC 2.3.1.28 (Chloramphenicol O-Acetyltransferase)

L64 ANSWER 11 OF 33 MEDLINE on STN
ACCESSION NUMBER: 1998073698 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9409233
TITLE: Thrombin stimulates **syndecan**-1 promotor activity and expression of a form of **syndecan**-1 that binds antithrombin III in vascular smooth muscle cells.
AUTHOR: Cizmeci-Smith G; Carey D J
CORPORATE SOURCE: Henry Hood MD Research Program, Sigfried, Pa., USA.
CONTRACT NUMBER: HL-48740 (NHLBI)
SOURCE: Arteriosclerosis, thrombosis, and vascular biology, (1997 Nov) 17 (11) 2609-16.
Journal code: 9505803. ISSN: 1079-5642.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U84896
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980130
Last Updated on STN: 19980130
Entered Medline: 19980122

ABSTRACT:

Vascular smooth muscle (VSM) cells express transmembrane proteoglycans of the ***syndecan*** gene family. We reported previously that the expression of ***syndecans*** by VSM cells is regulated by mitogens such as serum, platelet-derived growth factor, and basic fibroblast growth factor and that ***syndecan*** expression is induced after balloon injury in vivo. We now show that thrombin is a potent inducer of **syndecan**-1 expression in VSM cells. Transient transfection experiments with a rat **syndecan**-1 promoter construct demonstrated that thrombin stimulates transcription of the ***syndecan*** -1 gene. **Syndecan** expression in response to thrombin was not inhibited by downregulation of protein kinase C. Thrombin-induced ***syndecan*** -1 expression was dependent on tyrosine kinase activity. Calcium was necessary for **syndecan**-1 expression, but increasing the intracellular calcium levels was not sufficient to induce **syndecan**-1 expression. Analysis of antithrombin III (AT III) binding activity revealed that thrombin caused an increase in the synthesis of **syndecan**-1 molecules that exhibited high-affinity AT III binding. These results suggest that VSM cells could play an important role in controlling local thrombus formation subsequent to vascular injury, via a feedback mechanism that involves thrombin-induced stimulation of an inhibitor of thrombin activity.

CONTROLLED TERM: Check Tags: Comparative Study; Male
Animals
*Antithrombin III: ME, metabolism
Base Sequence
Calcium: PH, physiology
Cells, Cultured
Chelating Agents: PD, pharmacology
Egtazic Acid: AA, analogs & derivatives
Egtazic Acid: PD, pharmacology
Membrane Glycoproteins: BI, biosynthesis
*Membrane Glycoproteins: GE, genetics
Mice
Molecular Sequence Data
*Muscle, Smooth, Vascular: DE, drug effects
Muscle, Smooth, Vascular: ME, metabolism
Platelet-Derived Growth Factor: PD, pharmacology
*Promoter Regions (Genetics): DE, drug effects
Protein Kinase C: PH, physiology
Proteoglycans: BI, biosynthesis
*Proteoglycans: GE, genetics
RNA, Messenger: BI, biosynthesis
Rats
Rats, Sprague-Dawley
Recombinant Fusion Proteins: BI, biosynthesis
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Sequence Alignment
Sequence Homology, Nucleic Acid
Signal Transduction: DE, drug effects
Tetradecanoylphorbol Acetate: PD, pharmacology
*Thrombin: PD, pharmacology
Transfection

CAS REGISTRY NO.: 139890-68-9 (1,2-bis(2-aminophenoxy)ethane N,N,N',N'-tetraacetic acid acetoxymethyl ester); 16561-29-8 (Tetradecanoylphorbol Acetate); 67-42-5 (Egtazic Acid); 7440-70-2 (Calcium); 9000-94-6 (Antithrombin III)

CHEMICAL NAME: 0 (Chelating Agents); 0 (Membrane Glycoproteins); 0 (Platelet-Derived Growth Factor); 0 (Proteoglycans); 0 (RNA, Messenger); 0 (Recombinant Fusion Proteins); 0 (**syndecan**); EC 2.7.1.37 (Protein Kinase C); EC 3.4.21.5 (Thrombin)

Searched by Barb O'Bryen, STIC 2-2518

L64 ANSWER 12 OF 33 MEDLINE on STN
ACCESSION NUMBER: 97439784 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9294130
TITLE: The **syndecan** family of proteoglycans. Novel receptors mediating internalization of atherogenic lipoproteins in vitro.
AUTHOR: Fuki I V; Kuhn K M; Lomazov I R; Rothman V L; Tuszynski G P; Iozzo R V; Swenson T L; Fisher E A; Williams K J
CORPORATE SOURCE: Department of Medicine, Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania 19107, USA.
CONTRACT NUMBER: CA39481 (NCI)
DK44498 (NIDDK)
HL38956 (NHLBI)
+
SOURCE: Journal of clinical investigation, (1997 Sep 15) 100 (6) 1611-22.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199712
ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971208

ABSTRACT:
Cell-surface heparan sulfate proteoglycans have been shown to participate in lipoprotein catabolism, but the roles of specific proteoglycan classes have not been examined previously. Here, we studied the involvement of the ***syndecan*** proteoglycan family. First, transfection of CHO cells with expression vectors for several **syndecan** core proteins produced parallel increases in the cell association and degradation of lipoproteins enriched in lipoprotein lipase, a heparan-binding protein. Second, a chimeric construct, FcR-Synd1, that consists of the ectodomain of the IgG Fc receptor Ia linked to the highly conserved transmembrane and cytoplasmic domains of ***syndecan*** -1 directly mediated efficient internalization, in a process triggered by ligand clustering. Third, internalization of lipase-enriched lipoproteins via **syndecan**-1 and of clustered IgGs via the chimera showed identical kinetics (t1/2 = 1 h) and identical dose-response sensitivities to cytochalasin B, which disrupts microfilaments, and to genistein, which inhibits tyrosine kinases. In contrast, internalization of the receptor-associated protein, which proceeds via coated pits, showed a t1/2 < 15 min, limited sensitivity to cytochalasin B, and complete insensitivity to genistein. Thus, **syndecan** proteoglycans can directly mediate ligand catabolism through a pathway with characteristics distinct from coated pits, and might act as receptors for atherogenic lipoproteins and other ligands in vivo.

CONTROLLED TERM:
Animals
CHO Cells
Chloroquine: PD, pharmacology
Cytochalasin B: PD, pharmacology
Dose-Response Relationship, Drug
Genistein: PD, pharmacology
Hamsters
Heparin: PD, pharmacology
Humans
LDL-Receptor Related Protein 1
Lipoprotein Lipase: ME, metabolism

Searched by Barb O'Bryen, STIC 2-2518

*Lipoproteins, LDL: ME, metabolism
Lipoproteins, LDL: PK, pharmacokinetics
Membrane Glycoproteins: GE, genetics
*Membrane Glycoproteins: ME, metabolism
Proteoglycans: GE, genetics
*Proteoglycans: ME, metabolism
Rats
Receptors, IgG: GE, genetics
Receptors, IgG: ME, metabolism
Receptors, Immunologic: PH, physiology
Receptors, LDL: PH, physiology
Recombinant Fusion Proteins: PD, pharmacology
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Thrombospondins: PD, pharmacology
Transfection

CAS REGISTRY NO.: 14930-96-2 (Cytochalasin B); 446-72-0 (Genistein); 54-05-7 (Chloroquine); 9005-49-6 (Heparin)

CHEMICAL NAME: 0 (LDL-Receptor Related Protein 1); 0 (Lipoproteins, LDL); 0 (Membrane Glycoproteins); 0 (Proteoglycans); 0 (Receptors, IgG); 0 (Receptors, Immunologic); 0 (Receptors, LDL); 0 (Recombinant Fusion Proteins); 0 (Thrombospondins); 0 (**syndecan**); EC 3.1.1.34 (Lipoprotein Lipase)

L64 ANSWER 13 OF 33 MEDLINE on STN
ACCESSION NUMBER: 96326680 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8707854
TITLE: Identification of stromal cell products that interact with pre-B cells.
AUTHOR: Oritani K; Kincade P W
CORPORATE SOURCE: Oklahoma Medical Research Foundation, Oklahoma City 73104, USA.
CONTRACT NUMBER: AI-33085 (NIAID)
SOURCE: Journal of cell biology, (1996 Aug) 134 (3) 771-82.
Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U47323
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19960919
Last Updated on STN: 19970203
Entered Medline: 19960912

ABSTRACT:
Our understanding of lympho-hematopoietic microenvironments is incomplete, and a new cloning strategy was developed to identify molecules that bind to B lineage lymphocyte precursors. A cell sorting procedure was used for initial enrichment of cDNAs from stromal cell mRNA that contained signal sequences and were therefore likely to encode transmembrane or secreted proteins. A second step involved expression of the library as soluble Ig fusion proteins. Finally, pools representing these proteins were screened for the ability to recognize pre-B cells. This approach resulted in the cloning of biglycan, ***syndecan*** 4, collagen type I, clusterin, matrix glycoprotein sc1, osteonectin, and one unknown molecule (designated SIM). The full-length cDNA of SIM revealed that it is a type I transmembrane protein, and its intracellular domain has weak homology with myosin heavy chain and related proteins. Staining of established cell lines and freshly isolated hematopoietic cells with the Ig fusion proteins revealed distinct patterns of reactivity and differential dependence on divalent cations. Biglycan-, sc1-,

and SIM-Ig fusion proteins selectively increased interleukin 7-dependent proliferation of pre-B cells. Overexpression of the entire SIM protein affected the morphology of 293T cells, while expression of just the extracellular portion was without effect. Thus, a series of stromal cell surface molecules has been identified that interact with blood cell precursors. Three of them promoted the survival and/or proliferation of pre-B cells in culture, and all merit further study in relation to lympho-hematopoiesis.

CONTROLLED TERM: Amino Acid Sequence
Animals
*B-Lymphocytes: ME, metabolism
Base Sequence
Cations, Divalent
Cell Line
*Cloning, Molecular: MT, methods
DNA, Complementary: GE, genetics
Gene Library
*Glycoproteins: GE, genetics
Glycoproteins: ME, metabolism
Humans
Interleukin-7: PH, physiology
Ligands
*Membrane Glycoproteins: GE, genetics
Membrane Glycoproteins: PH, physiology
Mice
Mice, Inbred BALB C
Molecular Sequence Data
Organ Specificity
Protein Binding
Protein Sorting Signals: GE, genetics
RNA, Messenger: AN, analysis
Recombinant Fusion Proteins: ME, metabolism
Recombinant Fusion Proteins: PD, pharmacology
Research Support, U.S. Gov't, P.H.S.
Sequence Homology, Amino Acid
*Stromal Cells
Tumor Cells, Cultured

CHEMICAL NAME: 0 (Cations, Divalent); 0 (DNA, Complementary); 0 (Glycoproteins); 0 (Interleukin-7); 0 (Ligands); 0 (Membrane Glycoproteins); 0 (Protein Sorting Signals); 0 (RNA, Messenger); 0 (Recombinant Fusion Proteins); 0 (Stim1 protein, mouse)

L64 ANSWER 14 OF 33 MEDLINE on STN
ACCESSION NUMBER: 96195282 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8609172
TITLE: Stimulation of fibroblast growth factor receptor-1 occupancy and signaling by cell surface-associated **syndecans** and glypican.
AUTHOR: Steinfeld R; Van Den Berghe H; David G
CORPORATE SOURCE: Center for Human Genetics, University of Leuven, Belgium.
SOURCE: Journal of cell biology, (1996 Apr) 133 (2) 405-16.
Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199605
ENTRY DATE: Entered STN: 19960605
Last Updated on STN: 19980206
Entered Medline: 19960530

ABSTRACT:
The formation of distinctive basic FGF-heparan sulfate complexes is essential for the binding of bFGF to its cognate receptor. In previous experiments, cell-surface heparan sulfate proteoglycans extracted from human lung fibroblasts could not be shown to promote high affinity binding of bFGF when added to heparan sulfate-deficient cells that express FGF receptor-1 (FGFR1) (Aviezer, D., D. Hecht, M. Safran, M. Eisinger, G. David, and A. Yayon. 1994. Cell 79:1005-1013). In alternative tests to establish whether cell-surface proteoglycans can support the formation of the required complexes, K562 cells were first transfected with the IIIc splice variant of FGFR1 and then transfected with constructs coding for either **syndecan**-1, ***syndecan*** -2, **syndecan**-4 or glypican, or with an antisense ***syndecan*** -4 construct. Cells cotransfected with receptor and proteoglycan showed a two- to three- fold increase in neutral salt-resistant specific 125I-bFGF binding in comparison to cells transfected with only receptor or cells cotransfected with receptor and anti-**syndecan**-4. Exogenous heparin enhanced the specific binding and affinity cross-linking of 125I-bFGF to FGFR1 in receptor transfectants that were not cotransfected with proteoglycan, but had no effect on this binding and decreased the yield of bFGFR cross-links in cells that were cotransfected with proteoglycan. Receptor-transfectant cells showed a decrease in glycophorin A expression when exposed to bFGF. This suppression was dose-dependent and obtained at significantly lower concentrations of bFGF in proteoglycan-cotransfected cells. Finally, complementary cell-free binding assays indicated that the affinity of 125I-bFGF for an immobilized FGFR1 ectodomain was increased threefold when the ***syndecan*** -4 ectodomain was coimmobilized with receptor. Equimolar amounts of soluble **syndecan**-4 ectodomain, in contrast, had no effect on this binding. We conclude that, at least in K562 cells, **syndecans** and glypican can support bFGF-FGFR1 interactions and signaling, and that cell-surface association may augment their effectiveness.

CONTROLLED TERM:
Antigens, CD14: AN, analysis
Base Sequence
Cell Differentiation
Cross-Linking Reagents
Fibroblast Growth Factor 2: GE, genetics
Fibroblast Growth Factor 2: ME, metabolism
Fibroblast Growth Factor 2: PD, pharmacology
Glycophorin: AN, analysis
Glycosaminoglycans: AN, analysis
Hematopoietic Stem Cells: CY, cytology
Heparan Sulfate Proteoglycan
Heparin: PD, pharmacology
Heparitin Sulfate: AN, analysis
Heparitin Sulfate: GE, genetics
Heparitin Sulfate: ME, metabolism
*Heparitin Sulfate: PH, physiology
Humans
Membrane Glycoproteins: GE, genetics
Membrane Glycoproteins: ME, metabolism
*Membrane Glycoproteins: PH, physiology
Molecular Sequence Data
Protein Binding
Proteoglycans: GE, genetics
Proteoglycans: ME, metabolism
*Proteoglycans: PH, physiology
*Receptor Protein-Tyrosine Kinases
Receptors, Fibroblast Growth Factor: GE, genetics
*Receptors, Fibroblast Growth Factor: ME, metabolism
Recombinant Fusion Proteins: IP, isolation & purification

Searched by Barb O'Bryen, STIC 2-2518

Recombinant Fusion Proteins: ME, metabolism
Research Support, Non-U.S. Gov't
*Signal Transduction: PH, physiology
Transfection
Tumor Cells, Cultured

CAS REGISTRY NO.: 103107-01-3 (Fibroblast Growth Factor 2); 9005-49-6 (Heparin); 9050-30-0 (Heparitin Sulfate)

CHEMICAL NAME: 0 (Antigens, CD14); 0 (Cross-Linking Reagents); 0 (Glycophorin); 0 (Glycosaminoglycans); 0 (Heparan Sulfate Proteoglycan); 0 (Membrane Glycoproteins); 0 (Proteoglycans); 0 (Receptors, Fibroblast Growth Factor); 0 (Recombinant Fusion Proteins); EC 2.7.1.112 (Receptor Protein-Tyrosine Kinases); EC 2.7.1.112 (fibroblast growth factor receptor 1)

L64 ANSWER 15 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:872836 CAPLUS
DOCUMENT NUMBER: 141:344591
TITLE: Rat Nogo-receptors and uses for preparing fusion proteins, antibody and modulating neurite outgrowth and treatment of central nervous system disorders
INVENTOR(S): Giger, Roman J.
PATENT ASSIGNEE(S): University of Rochester, USA
SOURCE: PCT Int. Appl., 156 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004090103	A2	20041021	WO 2004-US10328	20040402

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-460849P P 20030404
ED Entered STN: 21 Oct 2004
AB Disclosed are compns. relating to the Nogo receptor (NgR) family, including NgR2 and NgR3, as well as fragments, chimeras, and variants thereof. The invention provides polypeptides, nucleic acids, vectors, expression systems, and antibodies and antibody fragments related to the NgRs as well as uses thereof. Such uses include modulation neurite outgrowth in a subject and treatment of central nervous system disorders in a subject, as well as, methods of identifying and screening compds. that can be used for modulating neurite outgrowth in a subject or in treatment of central nervous system disorders in a subject.
IC ICM C12N
CC 3-2 (Biochemical Genetics)

Section cross-reference(s): 6, 13

IT **Syndecans**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(3; rat Nogo-receptors and uses for preparing **fusion protein**, antibody and modulating neurite outgrowth and treatment of central nervous system disorders)

IT **Syndecans**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(NgR interacting with; rat Nogo-receptors and uses for preparing **fusion protein**, antibody and modulating neurite outgrowth and treatment of central nervous system disorders)

IT Nerve **growth factor** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(low affinity, NgR2 interacting with; rat Nogo-receptors and uses for preparing fusion protein, antibody and modulating neurite outgrowth and treatment of central nervous system disorders)

IT **Fusion proteins (chimeric proteins)**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(rat Nogo-receptors and uses for preparing fusion protein, antibody and modulating neurite outgrowth and treatment of central nervous system disorders)

IT 9005-49-6, Heparin, biological studies 9050-30-0 11089-65-9, Tunicamycin 59247-13-1, Ganglioside GT1b 62031-54-3, Fibroblast **growth factor** 106096-92-8 106096-93-9, Fibroblast **growth factor** 2 123584-45-2, Fibroblast **growth factor** 4 148348-14-5, Fibroblast **growth factor** 3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(rat Nogo-receptors and uses for preparing fusion protein, antibody and modulating neurite outgrowth and treatment of central nervous system disorders)

L64 ANSWER 16 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 9
ACCESSION NUMBER: 2001:416975 CAPLUS
DOCUMENT NUMBER: 135:37179
TITLE: Proteoglycans and pharmaceutical compositions comprising them
INVENTOR(S): Yayon, Avner
PATENT ASSIGNEE(S): Yeda Research and Development Co. Ltd., Israel
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001040267	A2	20010607	WO 2000-IL821	20001205
WO 2001040267	A3	20020711		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,

BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1237922 A2 20020911 EP 2000-979926 20001205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
US 2003100492 A1 20030529 US 2002-149326 20020924
PRIORITY APPLN. INFO.: IL 1999-133318 A 19991205
WO 2000-IL821 W 20001205

ED Entered STN: 08 Jun 2001

AB A mol. is provided capable of promoting high-affinity binding of a fibroblast growth factor (FGF) to a FGF receptor (FGFR), said mol. being selected from: (i) a recombinant chimeric fusion mol. comprising the extracellular domain of a syndecan or a fragment thereof fused to a tag suitable for proteoglycan purification, said fusion mol. being post-translationally glycosylated to carry at least one chain of a heparan sulfate having at least one highly sulfated domain; (ii) a DNA sequence encoding a chimeric fusion mol. comprising the extracellular domain of a syndecan or a fragment thereof fused to a tag suitable for proteoglycan purification; and (iii) a sugar mol. from a syndecan carrying at least one chain of a heparan sulfate having at least one highly sulfated domain. The compds. may be used for induction of angiogenesis, bone fracture healing, enhancement of wound healing, promotion of tissue regeneration and treatment of ischemic heart diseases and peripheral vascular diseases.

IC ICM C07K014-00
CC 63-6 (Pharmaceuticals)

IT **Syndecans**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(proteoglycans and pharmaceutical compns. comprising them for cardiovascular and wound-healing applications)

IT **Fusion proteins (chimeric proteins)**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(proteoglycans and pharmaceutical compns. comprising them for cardiovascular and wound-healing applications)

IT Fibroblast **growth factor** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(proteoglycans and pharmaceutical compns. comprising them for cardiovascular and wound-healing applications)

IT Angiogenic factors
Hepatocyte **growth factor**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(proteoglycans and pharmaceutical compns. comprising them for cardiovascular and wound-healing applications)

IT **Syndecans**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(syndecans-1; proteoglycans and pharmaceutical compns. comprising them for cardiovascular and wound-healing applications)

IT **Syndecans**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(syndecans-2; proteoglycans and pharmaceutical compns. comprising them for cardiovascular and wound-healing applications)

IT **Syndecans**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(syndecans-3; proteoglycans and pharmaceutical compns. comprising them for cardiovascular and wound-healing applications)

IT **Syndecans**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(syndecans-4; proteoglycans and pharmaceutical compns. comprising them for cardiovascular and wound-healing applications)

IT Fibroblast **growth factor** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(type 1; proteoglycans and pharmaceutical compns. comprising them for cardiovascular and wound-healing applications)

IT Fibroblast **growth factor** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(type 2; proteoglycans and pharmaceutical compns. comprising them for cardiovascular and wound-healing applications)

IT Fibroblast **growth factor** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(type 3; proteoglycans and pharmaceutical compns. comprising them for cardiovascular and wound-healing applications)

IT **343431-95-8**, Syndecan-4 (mouse endothelium-derived)
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(amino acid sequence; proteoglycans and pharmaceutical compns. comprising them for cardiovascular and wound-healing applications)

IT 50812-37-8D, Glutathione S transferase, fusion proteins 62229-50-9, egf
127464-60-2, Vascular endothelial **growth factor**
148348-15-6, Fibroblast **growth factor** 7
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(proteoglycans and pharmaceutical compns. comprising them for cardiovascular and wound-healing applications)

L64 ANSWER 17 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 10
ACCESSION NUMBER: 2001:921790 CAPLUS
DOCUMENT NUMBER: 136:145425
TITLE: Engineering of a heparin-binding **growth factor** with heparan sulfate sugar chains
AUTHOR(S): Asada, Masahiro; Yoneda, Atsuko; Imamura, Toru
CORPORATE SOURCE: Gene Discovery Research Center, National Institute of Advanced Industrial Science and Technology(AIST), Ibaraki, 305-8566, Japan
SOURCE: Trends in Glycoscience and Glycotechnology (2001), 13(72), 385-394
CODEN: TGGLEE; ISSN: 0915-7352
PUBLISHER: FCCA
DOCUMENT TYPE: Journal
LANGUAGE: English/Japanese
ED Entered STN: 21 Dec 2001
AB Fibroblast growth factor (FGF) family members cannot exert their biol. activity in the absence of their interaction with heparan sulfate or heparin in the vicinity of their receptors. Cell surface proteoglycans are thought to serve such heparan sulfate sugar chains in physiol. conditions. In an attempt to utilize this interaction for engineering FGFs, the authors' aim was to construct an FGF neoglycoprotein with heparan sulfate sugar chains. A novel chimeric protein was designed in which part of syndecan-4 containing glycosaminoglycan (GAG) attachment sites was ligated to the N-terminus of FGF-1. When the cDNA encoding the protein was transfected into CHO-K1 cells, the chimeric protein was

secreted into the conditioned medium with GAG modifications. One fraction of the resultant chimeric protein had acquired the ability to stimulate DNA synthesis of the target cells in the absence of exogenous or cellular heparin/heparan sulfate, indicating that the biol. function of FGF-1 was successfully modified by this approach. Furthermore in artificial wound fluid which mimics inflammation, the activity of this protein was highly augmented due to the generation of small HS fragments which act as activators. These results suggest that engineering heparin-binding proteins with heparan sulfate sugar chains is highly effective.

CC 2-5 (Mammalian Hormones)

ST FGF1 heparin binding **growth factor** heparan sulfate sugar chain

IT **Syndecans**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(4; engineering of heparin-binding **growth factor** with heparan sulfate sugar chains)

IT **Fusion proteins (chimeric proteins)**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(PG-FGF1; engineering of heparin-binding **growth factor** with heparan sulfate sugar chains)

IT Genetic engineering
(engineering of heparin-binding **growth factor** with heparan sulfate sugar chains)

IT Carbohydrates, biological studies
Glycoproteins
Glycosaminoglycans, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(engineering of heparin-binding **growth factor** with heparan sulfate sugar chains)

IT Inflammation
(engineering of heparin-binding **growth factor** with heparan sulfate sugar chains in relation to augmentation of engineered FGF-1 in artificial wound fluid mimicking inflammation)

IT **Growth factors**, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(heparin-binding; engineering of heparin-binding **growth factor** with heparan sulfate sugar chains)

IT 9007-28-7, Chondroitin sulfate 9050-30-0, Heparan sulfate 106096-92-8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(engineering of heparin-binding **growth factor** with heparan sulfate sugar chains)

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L64 ANSWER 18 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 12

ACCESSION NUMBER: 1999:547509 CAPLUS

DOCUMENT NUMBER: 131:267259

TITLE: The role of syndecan cytoplasmic domain in basic fibroblast **growth factor**-dependent signal transduction

AUTHOR(S): Volk, Ruediger; Schwartz, John J.; Li, Jian; Rosenberg, Robert D.; Simons, Michael

CORPORATE SOURCE: Angiogenesis Research Center, Cardiovascular Division, Department of Medicine, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, 02215, USA

SOURCE: Journal of Biological Chemistry (1999), 274(34), 24417-24424
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 31 Aug 1999
AB To determine the role played by syndecan-4 cytoplasmic domain in the mediation of basic fibroblast growth factor (bFGF) signaling, immortalized human cells (ECV) were used to generate cell lines expressing constructs encoding full-length sequences for syndecan-4 (S4), syndecan-1 (S1), glypican-1 (G1), or chimeric proteins consisting of the ectoplasmic domain of glypican-1 linked to the transmembrane/cytoplasmic domain of syndecan-4 (G1-S4c) and the ectoplasmic domain of syndecan-4 linked to the glypican-1 glycosylphosphatidyl-inositol (GPI) anchor sequence (S4-GPI). Vector-transduced cells (VC) were used as controls. Expression of all these proteoglycans (except for the vector control) significantly increased cell-associated heparan sulfate mass and the number of low affinity bFGF-binding sites. However, in low serum medium, the addition of bFGF stimulated growth and migration of cells expressing S4 and G1-S4c constructs but not G1, S1, S4-GPI, or VC cells. Similar results were obtained using Matrigel growth assays. Mutations of heparan sulfate attachment sites on S4 construct abolished syndecan-4-dependent augmentation of bFGF responses. The authors conclude that cytoplasmic tail of syndecan-4 plays an important role in bFGF-mediated signal transduction.
CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 13
IT **Syndecans**
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(4; syndecan cytoplasmic domain role in basic fibroblast **growth factor**-dependent signal transduction)
IT Blood vessel
(endothelium; syndecan cytoplasmic domain role in basic fibroblast **growth factor**-dependent signal transduction)
IT Gene
(expression; syndecan cytoplasmic domain role in basic fibroblast **growth factor**-dependent signal transduction)
IT Proteoglycans, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(glypican-1; syndecan cytoplasmic domain role in basic fibroblast **growth factor**-dependent signal transduction)
IT Cell migration
Cell proliferation
Protein motifs
Signal transduction, biological
(syndecan cytoplasmic domain role in basic fibroblast **growth factor**-dependent signal transduction)
IT **Fusion proteins (chimeric proteins)**
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(syndecan-glypican; syndecan cytoplasmic domain role in basic fibroblast **growth factor**-dependent signal transduction)
IT **Syndecans**
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation,

nonpreparative); PROC (Process)
(syndecans-1; syndecan cytoplasmic domain role in basic fibroblast **growth factor**-dependent signal transduction)

IT 106096-93-9, Basic fibroblast **growth factor**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(syndecan cytoplasmic domain role in basic fibroblast **growth factor**-dependent signal transduction)

IT 9050-30-0, Heparan sulfate
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(syndecan cytoplasmic domain role in basic fibroblast **growth factor**-dependent signal transduction)

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L64 ANSWER 19 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:175824 CAPLUS
DOCUMENT NUMBER: 132:217982
TITLE: Stimulation of angiogenesis via enhanced endothelial expression of chimeric heparan sulfate-binding proteins
INVENTOR(S): Simons, Michael; Volk, Rudiger; Horowitz, Arie
PATENT ASSIGNEE(S): Beth Israel Deaconess Medical Center, USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000014103	A1	20000316	WO 1999-US18865		19990818
W: AU, CA, JP					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
US 6852515	B1	20050208	US 1998-145916		19980902
CA 2346430	AA	20000316	CA 1999-2346430		19990818
AU 9956794	A1	20000327	AU 1999-56794		19990818
EP 1112283	A1	20010704	EP 1999-943760		19990818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
US 2004013653	A1	20040122	US 2003-352839		20030128
PRIORITY APPLN. INFO.:			US 1998-145916	A	19980902
			WO 1999-US18865	W	19990818

ED Entered STN: 17 Mar 2000

AB The present invention provides tangible means and methods for stimulation of angiogenesis via enhanced endothelial expression of core proteins having a syndecan-4 cytoplasmic region intracellularly. The tangible means include a prepared DNA sequence fragment having sep. and individual DNA sequenced portions coding for an heparan sulfate-binding extracellular domain, a central transmembrane domain, and a cytoplasmic domain coding for the syndecan-4 polypeptide. The prepared DNA sequence unitary fragment may be delivered to endothelial cells in-situ , both under in-vivo and/or in-vitro conditions, using suitable expression vectors including plasmids and viruses. The resulting transfected endothelial cells overexpress heparan sulfate-binding core proteins, and the resulting overexpression of

these proteoglycan entities causes stimulation of angiogenesis in-situ.

IC ICM C07H021-04
ICS C12N015-63; C12N015-85; C12N015-08; C12N015-09; C12N015-00; A61K048-00

CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1, 6

IT **Syndecans**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(2, **fusion protein** comprising portions of; stimulation of angiogenesis via enhanced endothelial expression of **chimeric** heparan sulfate-binding **proteins** (proteoglycans))

IT **Syndecans**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(4, **fusion protein** comprising portions of; stimulation of angiogenesis via enhanced endothelial expression of **chimeric** heparan sulfate-binding **proteins** (proteoglycans))

IT **Proteins, specific or class**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(Glypican-1, fusion protein comprising portions of; stimulation of angiogenesis via enhanced endothelial expression of **chimeric** heparan sulfate-binding proteins (proteoglycans))

IT **Proteins, specific or class**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(extracellular matrix-associated, fusion protein comprising; stimulation of angiogenesis via enhanced endothelial expression of **chimeric** heparan sulfate-binding proteins (proteoglycans))

IT **Proteins, specific or class**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(ligand-binding; stimulation of angiogenesis via enhanced endothelial expression of **chimeric** heparan sulfate-binding proteins)

IT **Growth factor** receptors
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(pleiotrophin, fusion protein comprising portions of; stimulation of angiogenesis via enhanced endothelial expression of chimeric heparan sulfate-binding proteins (proteoglycans))

IT **Fusion proteins (chimeric proteins)**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(stimulation of angiogenesis via enhanced endothelial expression of chimeric heparan sulfate-binding proteins)

IT **Syndecans**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(syndecans-1, **fusion protein** comprising portions of; stimulation of angiogenesis via enhanced endothelial expression of **chimeric** heparan sulfate-binding **proteins** (proteoglycans))

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L64 ANSWER 20 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:123904 CAPLUS
DOCUMENT NUMBER: 124:336193
TITLE: Recombinantly produced syndecan-1, syndecan-1 fragments, and syndecan-1 fusion proteins
INVENTOR(S): Saunders, Scott; Bernfield, Merton; Kato, Masato
PATENT ASSIGNEE(S): Leland Stanford Junior University, USA; Children's Medical Center Corporation
SOURCE: U.S., 58 pp. Cont.-in-part of U.S. Ser. No. 757,654, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5486599	A	19960123	US 1993-78683	19930617
WO 9500633	A2	19950105	WO 1994-US6920	19940617
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9471129	A1	19950117	AU 1994-71129	19940617
EP 705332	A1	19960410	EP 1994-920272	19940617
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 6531295	B1	20030311	US 1995-471970	19950606
US 6699968	B1	20040302	US 2000-723677	20001128
PRIORITY APPLN. INFO.:			US 1989-331585 B2	19890329
			US 1991-746797 B2	19910812
			US 1991-757654 B2	19910906
			US 1992-856869 B2	19920324
			US 1993-78683 A	19930617
			WO 1994-US6920 W	19940617
			US 1995-471970 A1	19950606

ED Entered STN: 29 Feb 1996
AB Mouse syndecan-1 and soluble fragments of this protein produced by recombinant cells, and fusion proteins containing the heparan sulfate attachment sequence of syndecan-1 are claimed. Mouse mammary epithelial cell line NMuMG syndecan-1 cDNA and cloned, sequenced, and expressed in CHO cells. Northern blotting revealed two mRNA's of 2.6 and 3.4 kb in skin. liver, and mammary gland tissue. An unidentified 4.5 kb band was also found in cerebrum. Expression of antisense RNA to syndecan-1 in NMuMG cells caused a reduction in syndecan-1 expression and morphol. changes

in the cells. Soluble, truncated forms of syndecan-1 which were produced with recombinant CHO cells were found to have heparan sulfate and/or chondroitin sulfate attached. Sites of attachment of heparan sulfate and chondroitin sulfate in the amino terminal fragment of syndecan-1 were identified by site-directed mutagenesis.

IC ICM C07K014-435
ICS C07K019-00; C12N015-12; C12N015-62

NCL 530395000

CC 6-3 (General Biochemistry)
Section cross-reference(s): 3

IT **Proteoglycans, properties**
RL: BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(**syndecans-1**, recombinantly produced syndecan-1, syndecan-1 fragments, and syndecan-1 **fusion proteins**)

IT **162072-91-5P 163663-53-4P**, Syndecan 1 (mouse clone M-4-19B) **163663-54-5P 163663-55-6P** **163663-56-7P** 163663-62-5P 163663-64-7P
RL: BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(amino acid sequence; recombinantly produced syndecan-1, syndecan-1 fragments, and syndecan-1 **fusion proteins**)

IT **123339-86-6**, Syndecan (mouse clone 4-19B precursor **protein** moiety reduced)
RL: PRP (Properties)
(amino acid sequence; recombinantly produced syndecan-1, syndecan-1 fragments, and syndecan-1 **fusion proteins**)

L64 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:471840 CAPLUS
DOCUMENT NUMBER: 123:278073
TITLE: Construction and use of synthetic constructs encoding syndecan
INVENTOR(S): Saunders, Scott; Bernfield, Merton; Kato, Masato
PATENT ASSIGNEE(S): Children's Medical Center Corp., USA; Board of Trustees of the Leland Stanford Jr.
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9500633	A2	19950105	WO 1994-US6920	19940617
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5486599	A	19960123	US 1993-78683	19930617
AU 9471129	A1	19950117	AU 1994-71129	19940617
EP 705332	A1	19960410	EP 1994-920272	19940617
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.:
US 1993-78683 A 19930617
US 1989-331585 B2 19890329
US 1991-746797 B2 19910812
US 1991-757654 B2 19910906

US 1992-856869 B2 19920324
WO 1994-US6920 W 19940617

ED Entered STN: 08 Apr 1995

AB A purified mammalian proteoglycan, and genetic information encoding such proteoglycans, having a core polypeptide mol. weight of about 30 kD to about 35 kD, and comprising a hydrophilic amino terminal extracellular region, a hydrophilic carboxy terminal cytoplasmic region, a transmembrane hydrophobic region between said cytoplasmic and extracellular regions, a protease susceptible cleavage sequence extracellularly adjacent the transmembrane region of the peptide, and ≥1 glycosylation sites for attachment of a heparan sulfate chain to the extracellular region. The glycosylation site comprises a heparan sulfate attachment sequence represented by the formula: Xac-ZX-Ser-Gly-Ser-Gly, where Xac represents an amino acid residue having an acidic side chain, and Z represents form 1 to 10 amino acid residues. Addnl. peptides having this glycosylation site and genetic information useful for preparing a number of variations based on this glycosylation site are also provided. Mol. cloning of cDNA for syndecan-1 from NMuMG mouse mammary epithelial cells and uses of the soluble syndecan derivs. containing the heparan sulfate attachment sites in construction of chimeric functional proteins are disclosed. Preparation of syndecan-fibronectin chimera, syndecan-growth factor chimera, and syndecan-growth factor receptor chimera is also described.

IC ICM C12N005-10
ICS C12N001-21; C12N015-70; C12N015-85; C07K013-00; C12N015-12; C12N015-68; A61K037-02

ICA A61K043-00

CC 3-2 (Biochemical Genetics)
Section cross-reference(s): 1, 6

IT **123339-86-6P**, Syndecan (mouse clone 4-19B precursor **protein** moiety reduced) **162072-91-5P** **162072-93-7P** **163663-53-4P**, Syndecan 1 (mouse clone M-4-19B) **163663-54-5P** **163663-55-6P** **163663-56-7P**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; cloning of cDNA for syndecan-1 and use in construction of functional **fusion protein** containing heparan attachment site)

IT 162072-89-1P **163663-57-8P**
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heparan attachment site of syndecan-1; in construction of functional **fusion protein** containing heparan attachment site)

IT 162163-59-9P **163663-58-9P**
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heparan attachment site of syndecan-2; in construction of functional **fusion protein** containing heparan attachment site)

IT 162163-64-6P **163663-59-0P** **163663-60-3P** **163663-61-4P**
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heparan attachment site of syndecan-4; in construction of functional **fusion protein** containing heparan attachment site)

L64 ANSWER 22 OF 33 JICST-EPlus COPYRIGHT 2005 JST on STN
ACCESSION NUMBER: 1000828504 JICST-EPlus

TITLE: Activity modification of heparin binding **growth factor** FGF-1 by the **fusion** with **syndecan.**
AUTHOR: YONEDA ATSUKO; ASADA MASAHIRO; IMAMURA TOORU
CORPORATE SOURCE: Natl. Inst. of Bioscience and Human-Technol. Agency of Ind. Sci. and Technol.
SOURCE: Saibo Kogaku (Cell Technology), (2000) vol. 19, no. 9, pp. 1338-1340. Journal Code: Y0229A (Fig. 2, Ref. 2)
ISSN: 0287-3796
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Commentary
LANGUAGE: Japanese
STATUS: New
ABSTRACT:
To create fibroblast **growth factor** (FGF) independent of heparin and resistant to decomposition, a **chimera** molecule of FGF-1 binding with **syndecan**-4, one of heparan sulfate proteoglycans (HS-PG)s, at amino terminal was constructed. The cDNA of the **chimera** protein was intorduced into Chinese hamster ovary cell. The stable expression cell which was obtained secreted FGF-1 antibody reactive molecule, PG-FGF-1 as expected in supernatant from culture.

CLASSIFICATION: EB08090G; EC02050B (577.175.1; 575.113.089)
CONTROLLED TERM: FGF; hamster; cDNA; gene introduction; cell proliferation; proteoglycan
BROADER TERM: growth factor; bioactive factor; factor; Myomorpha; Rodentia; Mammalia; Vertebrata; animal; DNA; nucleic acid; gene manipulation; genetic technique; technology; operation(processing); cell physiology; multiplication(biology); polysaccharide; carbohydrate; glycoprotein; protein
SUPPLEMENTARY TERM: syndecan

L64 ANSWER 23 OF 33 JICST-EPlus COPYRIGHT 2005 JST on STN
ACCESSION NUMBER: 990584108 JICST-EPlus
TITLE: Proteoglycan Chimerization Augments Stability and Decreases Heparin Dependency of Fibroblast Growth Factor-1.
AUTHOR: ASADA MASAHIRO; ODA YUKO; YONEDA ATSUKO; OTA KEIKO; ORIKASA NORIKO; MIYAGAWA KAZUKO; SUZUKI MAKOTO; OKA SHUICHI; IMAMURA TOORU
CORPORATE SOURCE: Natl. Inst. of Bioscience and Human-Technol. Agency of Ind. Sci. and Technol.
SOURCE: Baiotekunoroji Shinpojiumu Yokoshu, (1998) vol. 16th, pp. 112-116. Journal Code: L0180A (Fig. 5, Ref. 6)
PUB. COUNTRY: Japan
DOCUMENT TYPE: Conference; Article
LANGUAGE: Japanese
STATUS: New
ABSTRACT:
Fibroblast **growth factor**(FGF)-1, or acidic FGF, is a member of heparin-binding FGF family. Heparin(HP) and heparan sulfate(HS) are especially important for FGF-1 to establish its full biological activities. To get insight into the mechanism of this HP/HS involvement and to obtain FGF-1 that is fully active without HP/HS, we constructed a proteoglycan-FGF-1 ***chimeric*** protein. The **chimera**, designated as GAG/FGF-1, was expressed by CHO cells that had been stably transfected with a **chimeric** cDNA encoding the ectodomain of **syndecan** and FGF-1. The expressed GAG/FGF-1 was recovered from the medium and was found to bind heparin-Sepharose by various affinities. Molecular mass of GAG/FGF-1 ranged from 100- to 200-kDa as revealed by FGF-1 immunoreactivity. Digestion with several glycosidases

confirmed the presence of GAG chains in GAG/FGF-1. As a mitogen, GAG/FGF-1 was similarly potent both in the presence and absence of heparin. Treatments of GAG/FGF-1 with acid, alkaline and heat followed by bioassay indicated that it is more resistant to these treatments than wild-type FGF-1. Thus, ***chimerization*** with proteoglycan yielded a novel artificial ***growth*** **factor** with augmented stability and less heparin-dependency. (author abst.)

CLASSIFICATION: CF02030M; EB03010N (544.412.1/.2:547; 577.112)
CONTROLLED TERM: FGF; glycosaminoglycan; heparin; proteoglycan; chimera; heparan sulfate; chondroitin sulfate; thermal stability; glycoxylation; cell proliferation; signal peptide; cDNA; vector(genetics); CHO cell; gene expression
BROADER TERM: growth factor; bioactive factor; factor; mucopolysaccharide; amino sugar; carbohydrate; polysaccharide; glucoside; glycoside; anticoagulant; hematological drug; drug; sugar sulfate; polyuronide; glycoprotein; protein; mosaic; carboxamide; aliphatic carboxylic acid; carboxylic acid; pyranoside; inorganic acid ester; ester; sulfuric acid derivative; sulfur oxyacid derivative; sulfur compound; oxygen group element compound; stability; condensation reaction; chemical reaction; cell physiology; multiplication(biology); peptide; DNA; nucleic acid; fibroblast; blast cell; cell(cytology); cultured cell; molecular genetic phenomenon; genetic phenomenon; phenomenon
SUPPLEMENTARY TERM: syndecan

L64 ANSWER 24 OF 33 PASCAL COPYRIGHT 2005 INIST-CNRS. ALL RIGHTS RESERVED. on STN DUPLICATE 8
ACCESSION NUMBER: 2002-0582204 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2002 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): FGF-2 interaction in breast cancer and benign mammary gland tissue
TITLE (IN GERMAN): FGF-2-Interaktionen in Mammakarzinomen und gesundem Brustdruesengewebe
AUTHOR: MUNDHENKE C.; MAASS N.; JONAT W.; FRIEDL A.
CORPORATE SOURCE: Frauenklinik der Christian-Albrechts Universitaet Kiel, Germany, Federal Republic of; Department of Pathology and Laboratory Medicine, University of Wisconsin, Madison, WI, United States
SOURCE: Geburtshilfe und Frauenheilkunde, (2002), 62(10), 962-966, 13 refs.
ISSN: 0016-5751 CODEN: GEFRA2
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: Germany, Federal Republic of
LANGUAGE: German
SUMMARY LANGUAGE: English
AVAILABILITY: INIST-4872, 354000106651080030
ABSTRACT: Purpose: FGF-2 is a mitogen for many cell types. Stimulation of breast carcinoma cell proliferation by this **growth factor** has been reported. FGF-2 binding to its receptor tyrosine kinases (RTK) and cellular signaling are modulated by heparan sulfate proteoglycans (HSPGs). The role of these molecules in breast carcinoma growth control is unknown. HSPG alterations in breast carcinomas compared to normal mammary gland should be

investigated. Material and Methods: 30 infiltrating breast carcinomas were examined. The ability of HSPGs to promote FGF-2 signaling complex assembly was tested. A FGF-2 ligand and a soluble RTK **fusion** protein (FR 1-AP) were used as binding probes. HSPG expression was measured by immunohistochemical detection of **syndecan**-1, **syndecan**-4 and glypican-1. Results: Other than normal gland epithelium, carcinoma cell HSPGs show increased FGF-2 binding. HSPG/FGF-2 complexes immobilize soluble FR 1-AP **fusion** protein, indicating that HSPGs promote FGF-2 signaling. Surprisingly, no single HSPG core protein co-localizes with this binding activity. **Syndecan**-1 is uniformly present in normal gland epithelium, but heterogeneously expressed in carcinomas. **Syndecan**-4 is highly expressed in normal gland epithelium, but reduced or lost in most carcinomas. It is lower in infiltrating than in in situ components, if both co-exist. No dramatic changes in glypican-1 expression are observed. Loss of **syndecan**-4 may convey an infiltrating, migratory phenotype to the carcinoma cells. Conclusion: The increased ability of carcinoma HSPG to promote FGF-2 signaling complex assembly is likely due to structural abnormalities of HS chains rather than altered core protein expression and may contribute to accelerated proliferation.

CLASSIFICATION CODE: 002B20E02; Life sciences; Medical sciences; Breast diseases, Breast; Oncology

CONTROLLED TERM: Carcinoma; Breast; Cell culture; Proteoglycan; Biological activity; Fibroblast growth factor; Binding; Immunohistochemistry; Cell proliferation; Human; Female

BROADER TERM: Malignant tumor; Breast disease; Growth factor; Cytokine; Polypeptide; Pathology

L64 ANSWER 25 OF 33 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 2003:36801215 BIOTECHNO

TITLE: Differential roles of two N-acetylgalactosaminyltransferases, CSGalNAcT-1, and a novel enzyme, CSGalNAcT-2. Initiation and elongation in synthesis of chondroitin sulfate

AUTHOR: Sato T.; Gotoh M.; Kiyohara K.; Akashima T.; Iwasaki H.; Kameyama A.; Mochizuki H.; Yada T.; Inaba N.; Togayachi A.; Kudo T.; Asada M.; Watanabe H.; Imamura T.; Kimata K.; Narimatsu H.

CORPORATE SOURCE: H. Narimatsu, Glycogene Function Team, Res. Center for Glycoscience (RCG), Natl. Inst. of Adv. Indust. Sci./T., Central-2 C-2, 1-1-1 Umezono, Tsukuba, Ibaraki 305-8568, Japan.
E-mail: h.narimatsu@aist.go.jp

SOURCE: Journal of Biological Chemistry, (31 JAN 2003), 278/5 (3063-3071), 47 reference(s)
CODEN: JBCHA3 ISSN: 0021-9258

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: By a tblastn search with β1,4-

galactosyltransferases as query sequences, we found an expressed sequence tag that showed similarity in β1,4-glycosyltransferase motifs. The full-length complementary DNA was obtained by a method of 5'-rapid amplification of complementary DNA ends. The predicted open reading frame encodes a typical type II membrane protein comprising 543 amino acids, the sequence of which was highly homologous to chondroitin sulfate N-acetylgalactosaminyltransferase (CSGalNAcT-1), and we designated this novel enzyme CSGalNAcT-2. CSGalNAcT-2 showed much stronger N-acetylgalactosaminyltransferase activity toward glucuronic acid of chondroitin poly- and oligosaccharides, and chondroitin sulfate poly- and oligosaccharides with a β1-4 linkage, i.e. elongation activity for chondroitin and chondroitin sulfate, but showed much weaker activity toward a tetrasaccharide of the glycosaminoglycan linkage structure (GlcA-Gal-Gal-Xyl-O-methoxyphenyl), i.e. initiation activity, than CSGalNAcT-1. Transfection of the CSGalNAcT-1 gene into Chinese hamster ovary cells yielded a change of glycosaminoglycan composition, i.e. the replacement of heparan sulfate on a **syndecan**-4/fibroblast **growth factor**-1 **chimera** protein by chondroitin sulfate, however, transfection of the CSGalNAcT-2 gene did not. The above results indicated that CSGalNAcT-1 is involved in the initiation of chondroitin sulfate synthesis, whereas CSGalNAcT-2 participates mainly in the elongation, not initiation. Quantitative real-time PCR analysis revealed that CSGalNAcT-2 transcripts were highly expressed in the small intestine, leukocytes, and spleen, however, both CSGalNAcTs were ubiquitously expressed in various tissues.

CONTROLLED TERM: *enzyme analysis; *enzyme activity; *biosynthesis; *nucleotide sequence; *n acetylgalactosaminyltransfera se; *chondroitin sulfate N acetylgalactosaminyltransferase 1; *chondroitin sulfate N acetylgalactosaminyltransferase 2; *chondroitin sulfate; expressed sequence tag; gene amplification; open reading frame; amino acid sequence; sequence homology; polymerase chain reaction; small intestine; leukocyte; spleen; protein expression; CHO cell; genetic transfection; quantitative analysis; human; article; priority journal; complementary DNA; membrane protein; amino acid; glucuronic acid; polysaccharide; oligosaccharide; glycosaminoglycan; heparan sulfate; syndecan; syndecan 4; fibroblast growth factor 1; unclassified drug

CAS REGISTRY NUMBER: (n acetylgalactosaminyltransferase) 9054-44-8; (chondroitin sulfate) 9007-28-7, 9082-07-9; (amino acid) 65072-01-7; (glucuronic acid) 36116-79-7, 576-37-4, 6556-12-3; (heparan sulfate) 9050-30-0

GENE NUMBER: GENBANK AB079252 submitted number; GENBANK AC011890 referred number; GENBANK NM018590 referred number

L64 ANSWER 26 OF 33 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
DUPLICATE

Searched by Barb O'Bryen, STIC 2-2518

ACCESSION NUMBER: 1999:30026854 BIOTECHNO
TITLE: Antisense inhibition of syndecan-3 expression during skeletal muscle differentiation accelerates myogenesis through a basic fibroblast growth factor-dependent mechanism
AUTHOR: Fuentealba L.; Carey D.J.; Brandan E.
CORPORATE SOURCE: E. Brandan, Depto. de Biologia Celular y Molec., Facultad de Ciencias Biologicas, P. Universidad Catolica de Chile, Casilla 114-D, Santiago, Chile. E-mail: ebrandan@genes.bio.puc.cl
SOURCE: Journal of Biological Chemistry, (31 DEC 1999), 274/53 (37876-37884), 44 reference(s)
CODEN: JBCHA3 ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT: **Syndecan**-3 is a member of a family of transmembrane proteoglycans that posses highly homologous cytoplasmic and transmembrane domains and function as extracellular matrix receptors and low-affinity receptors for signaling molecules such as basic fibroblasts **growth factor** (FGF-2). **Syndecan**-3 is transiently expressed in developing limb bud and absent in adult skeletal muscle. In this study we investigated the expression of **syndecan**-3 and its role on FGF-2-dependent inhibition of myogenesis. **Syndecan**-3 expression was down-regulated during skeletal muscle differentiation of C.sub.2C.sub.1.sub.2 myoblasts, as determined by Northern blot analyses and immunoprecipitation. To probe the function of **syndecan**-3 during myogenesis, C.sub.2C.sub.1.sub.2 myoblasts were stably transfected with a plasmid coding for antisense **syndecan**-3 mRNA. The resulting inhibition of **syndecan**-3 expression caused accelerated skeletal muscle differentiation, as determined by expression of creatine kinase and myosin and myoblast **fusion.** Expression of a master transcription factor for muscle differentiation, myogenin, was also accelerated in antisense **syndecan**-3-transfected myoblasts compared with control transfected and wild type cells. Reduced expression of **syndecan**-3 resulted in a 13-fold decrease in sensitivity to FGF-2-dependent inhibition of myogenin expression. Addition of heparin partially reversed this effect. These results demonstrate that **syndecan**-3 expression is down-regulated during differentiation and the level of expression of membrane-bound heparan sulfate on myoblast surface is critical for fine modulation of responsiveness to FGF-2. These findings strongly suggest a role for **syndecan**-3 in regulation of skeletal muscle terminal differentiation.
CONTROLLED TERM: *syndecan; *basic fibroblast growth factor; *protein expression; *muscle development; *skeletal muscle; *protein synthesis inhibition; myogenin; creatine kinase; myosin; fibroblast growth factor 2; heparan sulfate; down regulation; myoblast; gene expression;

genetic transfection; cell fusion; cell differentiation; nonhuman; mouse; controlled study; animal cell; article; priority journal

CAS REGISTRY NUMBER: (basic fibroblast growth factor) 106096-93-9; (myogenin) 127385-49-3; (creatine kinase) 9001-15-4; (heparan sulfate) 9050-30-0

L64 ANSWER 27 OF 33 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 1994:24233447 BIOTECHNO

TITLE: Amino acid determinants that drive heparan sulfate assembly in a proteoglycan

AUTHOR: Zhang L.; Esko J.D.

CORPORATE SOURCE: Biochemistry/Molec. Genetics Dept., Schools of Medicine and Dentistry, University of Alabama,Birmingham, AL 35294, United States.

SOURCE: Journal of Biological Chemistry, (1994), 269/30 (19295-19299)
CODEN: JBCHA3 ISSN: 0021-9258

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: To study how cells regulate the composition of glycosaminoglycan chains on proteoglycans, we have examined the assembly of chains on **chimeric** proteoglycans containing segments of betaglycan (transforming **growth factor**-β Type III receptors) **fused** to protein A. Transient expression of the **chimeras** in Chinese hamster ovary cells revealed that only two glycosaminoglycan attachment sites exist. One site at Ser.sup.5.sup.3.sup.5 supported both chondroitin sulfate and heparan sulfate synthesis, whereas the site at Ser.sup.5.sup.4.sup.6 supported only chondroitin sulfate. The compositions of the **chimeras** were the same in CHO-K1, CHOP-C4, BHK-21, and HeLa S3 cells and in **chimeras** containing polyhistidine **fused** to the C terminus. Deletion experiments showed that the assembly of heparan sulfate chains on the **chimeras** required a peptide segment of <=16 amino acids (SPGDSS.sup.5.sup.3.sup.5- GWPDGYEDLE) and the first 5 amino acids were not essential. Truncation of the acidic cluster (EDLE), site-directed mutation of the acidic residues in the cluster, or deletion of the sequence between the cluster and the Ser attachment site decreased heparan sulfate assembly. Mutation of Trp.sup.5.sup.3.sup.7 adjacent to the site also decreased heparan sulfate assembly. More importantly, introducing tryptophan next to three different Ser-Gly dipeptides in betaglycan and **syndecan**-1 **chimeras** stimulated assembly of heparan sulfate. Thus, one type of heparan sulfate attachment site consists of a Ser-Gly dipeptide and a flanking cluster of acidic residues. An adjacent tryptophan residue can augment the proportion of heparan sulfate.

CONTROLLED TERM: *growth factor receptor; *chondroitin sulfate; *heparan sulfate; *protein a; *proteoglycan; *serine;

*tryptophan; amino acid; hybrid protein; amino acid sequence; animal cell; article; binding site; carboxy terminal sequence; chimera; cho cell; nonhuman; polymerase chain reaction; priority journal; rat; site directed mutagenesis

CAS REGISTRY NUMBER: (chondroitin sulfate) 9007-28-7, 9082-07-9; (heparan sulfate) 9050-30-0; (serine) 56-45-1, 6898-95-9; (tryptophan) 6912-86-3, 73-22-3; (amino acid) 65072-01-7

L64 ANSWER 28 OF 33 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 1994:24026631 BIOTECHNO

TITLE: Differential structural requirements of heparin and heparan sulfate proteoglycans that promote binding of basic fibroblast growth factor to its receptor

AUTHOR: Aviezer D.; Levy E.; Safran M.; Svahn C.; Buddecke E.; Schmidt A.; David G.; Vlodavsky I.; Yayon A.

CORPORATE SOURCE: Dept. of Chemical Immunology, Weizmann Institute of Science,Rehovot 76100, Israel.

SOURCE: Journal of Biological Chemistry, (1994), 269/1 (114-121)
CODEN: JBCHA3 ISSN: 0021-9258

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: Heparan sulfate proteoglycans (HSPG) are obligatory for receptor binding and mitogenic activity of basic fibroblast **growth factor** (bFGF).
The capacity of various species of heparin and heparan sulfate (HS) to promote bFGF receptor binding was investigated using both Chinese hamster ovary mutant cells deficient in cell surface HSPG and a soluble bFGF receptor-alkaline phosphatase **fusion** protein. Highly sulfated oligosaccharides were more effective than medium and low sulfate fractions of the same size oligosaccharide. O-Sulfation in heparin was found to be critical for its capacity to promote binding of bFGF to its receptors. The highest level of bFGF-receptor binding was achieved in the presence of over-sulfated heparin fragments (% sulfur >14) regardless of whether the N-position was sulfated or acetylated. Unlike receptor binding of bFGF which requires oligosaccharides containing at least 8-10 sugar units, displacement of heparin- or HS-bound bFGF was obtained by oligosaccharides containing as little as four sugar units and by an N-sulfated, O-desulfated heparin fragment (% sulfur = 5.3). A preparation of total cell surface-derived HS induced bFGF receptor binding. A preliminary survey of several defined and affinity purified species of cell surface HSPG, including **syndecan**, fibroglycan, and glypican failed to identify natural HSPG that promote high affinity receptor binding of bFGF. A similar lack of activity was observed with species of HS isolated from bovine arterial tissue and characterized for their effect on vascular smooth muscle cell proliferation. Moreover, most of these species of HS inhibited in a dose-dependent manner the restoration

of bFGF-receptor binding induced by heparin or by total HSPG. These results suggest the involvement of defined heparin-like oligosaccharide sequences and unique species of cell surface and extracellular matrix HS in the regulation of bFGF receptor binding and biological activity.

CONTROLLED TERM: *fibroblast growth factor receptor; *basic fibroblast growth factor; *heparin; *proteoheparan sulfate; oligosaccharide; syndecan; animal cell; article; cattle; cho cell; drug acetylation; drug receptor binding; drug sulfation; endothelium cell; fetus; fetus lung; fibroblast; human; human cell; nonhuman; priority journal

CAS REGISTRY NUMBER: (basic fibroblast growth factor) 106096-93-9; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5

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ACCESSION NUMBER: 2004256396 ESBIOBASE

TITLE: Mammalian and Drosophila cells adhere to the laminin α4 LG4 domain through syndecans, but not glypicans

AUTHOR: Yamashita H.; Goto A.; Kadowaki T.; Kitagawa Y.

CORPORATE SOURCE: Y. Kitagawa, Grad. Courses for Reg. Biol. Signals, Grad. Sch. of Bioagricultural Sci., Nagoya University, Nagoya 464-8601, Japan.
E-mail: yasuok@agr.nagoya-u.ac.jp

SOURCE: Biochemical Journal, (15 SEP 2004), 382/3 (933-943), 47 reference(s)
CODEN: BIJOAK ISSN: 0264-6021

DOCUMENT TYPE: Journal; Article

COUNTRY: United Kingdom

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: We have previously shown that the LG4 (laminin G-like) domain of the laminin α4 chain is responsible for the significantly higher affinity of the α4 chain to heparin than found for other α chains [Yamaguchi, Yamashita, Mori, Okazaki, Nomizu, Beck and Kitagawa (2000) J. Biol. Chemical 275, 29458-29465]; four basic residues were identified to be essential for this activity [Yamashita, Beck and Kitagawa (2004) J. Mol. Biol. 335, 1145-1149]. By creating GST (glutathione S-transferase)-**fused** LG1, LG2, LG4 and LG5 proteins, we found that only LG4 is active for the adhesion of human HT1080 cells, human umbilical vein endothelial cells and Drosophila haemocytes Kc167 with a half-saturating concentration of 20 μg/ml. Adhesion was counteracted by treatment of the cells with heparin, heparan sulphate and heparitinase I. Upon mutating the four basic residues essential for heparin binding within LG4, the adhesion activity was abolished. Pull-down experiments using glutathione beads/GST-**fusion** proteins indicate a direct interaction of LG4 with **syndecan**-4, which might be the major receptor for cell adhesion. Neither the release of glypican-1 by treating human cells with phosphatidylinositol-specific phospholipase C nor targeted knockdown of dally or dally-like protein impaired the cell-adhesion

activity. As the LG4-LG5 domain of the α4 chain is cleaved in vivo from the main body of laminin-8 (α4β1γ1), we suggest that the heparan sulphate proteoglycan-binding activity of LG4 is significant in modulating the signalling of Wnt, Decapentaplegic and fibroblast **growth factors.**

CLASSIFICATION CODE: 89.1.4.5 CELL AND DEVELOPMENTAL BIOLOGY: MEMBRANES AND CELL TRANSPORT: Cell Junctions and Cell Adhesion: Adhesion molecules
89.4.1.1 CELL AND DEVELOPMENTAL BIOLOGY: EXTRACELLULAR MATRIX (STRUCTURE AND FUNCTION): Extracellular Matrix: Structure and composition
89.5.1 CELL AND DEVELOPMENTAL BIOLOGY: CELL TYPES AND BIOLOGY: Cell Types

SUPPLEMENTARY TERM: Heparin; Laminin; RNA interference; Syndecans

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DUPLICATE 2

ACCESSION NUMBER: 2004-08081 BIOTECHDS

TITLE: Inhibiting neuronal cell death using neuronal marker genes and proteins, useful for diagnosing, preventing and/or treating optic nerve degeneration, Alzheimer's disease, diabetic retinopathy, Parkinson's disease and glaucoma; involving vector-mediated gene transfer and expression in host cell for use in gene therapy

AUTHOR: ZACK D J; QUIGLEY H A

PATENT ASSIGNEE: UNIV JOHNS HOPKINS

PATENT INFO: WO 2004007675 22 Jan 2004

APPLICATION INFO: WO 2003-US21738 14 Jul 2003

PRIORITY INFO: US 2002-395821 15 Jul 2002; US 2002-395821 15 Jul 2002

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2004-122916 [12]

ABSTRACT: DERWENT ABSTRACT:
NOVELTY - Inhibiting neuronal cell death comprises administering to a subject an isolated molecule comprising an antibody variable region which specifically binds to a neuronal marker (NM1) protein, whereby neuronal cell death is inhibited.

DETAILED DESCRIPTION - The neuronal marker (NM1) protein in the method cited above is microglobulin, beta-2-microglobulin + prostaglandin receptor F2a, glutathione S-transferase Yb subunit, GST subunit 4 mu (GSTM2), vascular cell adhesion protein 1 precursor (V-CAM 1), gamma-aminobutyric acid (GABA) transporter 2, VGF8A protein precursor, Transforming **growth factor** beta (TGF-beta) masking protein large subunit, erythropoietin precursor (EPO), protein arginine N-methyltransferase 1, signal transducer and activator of transcription 3 (STATS), ceruloplasmin precursor (CP), ferroxidase, clusterin (CLU), testosterone-repressed prostate message 2 (TRPM2), apolipoprotein J, sulfated glycoprotein 2 (SGP2), dimeric acid glycoprotein (DAG), heparin-binding **growth factor** 2 precursor (HBGF2), basic fibroblast **growth factor** (BFGF), fibroblast **growth factor** 2 (FGF2), prostatropin, or plasminogen activator inhibitor 2A.
INDEPENDENT CLAIMS are also included for the following: (1) a method of preventing neuronal cell death in a mammal,

comprising administering to the mammal a nucleic acid molecule comprising a coding sequence for a neuronal marker (NM2) protein and/or the NM2 protein, whereby neuronal cell death in the mammal is inhibited or prevented; (2) method of identifying regions of neuronal cell death in a patient, comprising administering to a patient a molecule comprising an antibody variable region which specifically binds to NM1 protein, wherein the molecule is bound to a detectable moiety, and detecting the detectable moiety in the patient, thereby identifying regions of neuronal cell death; (3) a method of screening for neuronal cell death in a patient, comprising contacting a body fluid collected from the patient with a molecule comprising an antibody variable region which specifically binds to NM1 protein, or detecting an NM1 protein or a nucleic acid encoding the NM1 protein in a body fluid collected from the patient, wherein detection of cross-reactive material in the body fluid with the molecule indicates neuronal cell death in the patient; (4) a method of promoting neuronal cell death in a patient, comprising administering to a patient in need of neuronal cell death an NM1 protein or a nucleic acid molecule encoding the NM1 protein, whereby neuronal cell death in the patient is stimulated; and (5) a method to identify candidate drugs for treating neuronal cell death, comprising contacting cells which express one or more NM1 and/or NM2 genes and/or proteins with a test compound, determining expression or activity of the one or more NM1 genes and/or proteins by hybridization of mRNA of the cells to a nucleic acid probe which is complementary to the mRNA, and identifying a test compound as a candidate drug for treating neuronal cell death if it decreases expression or activity of the one and/or more NM1 and/or NM2 genes or proteins.

WIDER DISCLOSURE - Also disclosed are NM nucleic acids, polypeptides, host cells, vectors and antibodies used in the methods of the invention.

BIOTECHNOLOGY - Preferred Method: The NM2 protein is NM androgen binding protein, plasma kallikrein (rPK), Lim-2, embryonic motor neuron topographic organizer, HOMEOBOX PROTEIN LM-2 (LM/HOMEODOMAIN PROTEIN LHX5), DCC, netrin receptor, immunoglobulin gene superfamily member, former tumor suppressor protein candidate, N-myc proto-oncogene protein, M-phase inducer phosphatase 2 (MPI2), cell division control protein 25 B (CDC25B), von ebner's gland protein 2, VEG protein 2, VEGP2 + von ebner's gland protein 1, VEG protein 1, VEGP1, VEGP, synaptobrevin 1 (SYB1), vesicle-associated membrane protein 1 (VAMP1), 3-methylcholanthrene-inducible cytochrome P450 (P450MC), cytochrome P450 IA1 (CYPIA1), cytochrome P450 VU (CYP7), cholesterol 7-alpha-monooxygenase, cholesterol 7-alpha-hydroxylase, cyclic nucleotide-activated channel, olfactory, cytochrome P450 2E1 (CYP2E1), P450-J, P450RLM6, high affinity L-proline transporter, neuronal acetylcholine receptor protein alpha-3 chain precursor, sodium channel I, voltage-dependent L-type calcium channel alpha 1C subunit (CACNA1), cardiac muscle L-type calcium channel alpha 1 polypeptide isoform 1 (CCHL1A1), rat brain class C (RBC), CACH2, CACN2, ATPase, hydrogen-potassium, alpha 2a subunit, sodium channel, amiloride sensitive, alpha subunit, SCNEA, alpha NACH, SCNN1A, RENAC, cardiac specific sodium channel alpha subunit, potassium channel protein CDRK, neuronal

acetylcholine receptor protein alpha 5 subunit precursor (CHRNA5, ACRA5), sodium channel SHRSPHD, gamma subunit, epithelial, sodium channel protein 6 (SCP6), renal organic anion transporter (ROAT1) + multispecific organic anion transporter (OAT1), neuronal acetylcholine receptor protein alpha 6 subunit precursor (CHRNA6, ACRA6), purinergic receptor P2X3, ligand-gated ion channel, calcium channel, alpha 1 beta, sodium channel, beta 1 subunit, neuronal acetylcholine receptor protein alpha 7 subunit precursor (CHRNA7, ACRA7), neuronal nicotinic acetylcholine receptor alpha 2 subunit, proton gated cation channel drasic, sensory neuron specific, channel-inducing factor precursor (CHIP), corticosteroid-induced protein, MYELM BASIC PROTEIN S (MBPS), organic cation transporter 2 (OCT2), ASIC1 proton gated cation channel, glycine receptor alpha 3 subunit precursor (GLRA3), voltage-gated K+ channel protein, RK5, potassium channel protein, voltage-activated calcium channel alpha-1 subunit (RBE-II), nickel-sensitive T-type calcium channel alpha-1 subunit, inward rectifier potassium channel subfamily J member 2 (KCNJ2), RBL-IRK1, eek proto-oncogene, protein tyrosine kinase, eph/elk-related, prostaglandin D2 receptor, activin receptor type I precursor (ACVR1, ACTR1), serine/threonine-protein kinase receptor R1 (SKR1), TGF-B superfamily receptor type I (TSR-I), ACVRLK2, calcitonin receptor precursor (CT-R), C1AJC1E, prostaglandin E2 receptor EP2 subtype (PGE receptor EP2 subtype, PTGER2), prostanoid EP2 receptor, NEUREXINI-BETA PRECURSOR, Non-processed neurexin I-beta Synaptic cell surface proteins + NEUREXIN I-ALPHA PRECURSOR, Non-processed neurexin I-alpha Synaptic cell surface proteins, gastrin-releasing peptide precursor (GRP), neuromedin C, serotonin receptor, 5-hydroxytryptamine 6 receptor (5-HT-6), ST-B17, possesses high affinity for tricyclic psychotropic drugs, platelet activating factor receptor, alpha 2B adrenergic receptor (ADRA2B), alpha 2B adrenoceptor, VASOACTIVE INTESTINAL POLYPEPTIDE RECEPTOR 2 PRECURSOR (VIP-R-2) (PITUITARY ADENYLATE CYCLASE ACTIVATING POLYPEPTIDE TYPE M RECEPTOR) (PACAP TYPE M RECEPTOR) PACAP-R-3), transforming **growth factor** beta 3 (TGF-beta3), antiproliferative **growth factor**, vasopressin V1b receptor, prostaglandin E2 receptor EP4 subtype, alpha 2C adrenergic receptor (ADRA2C), alpha 2C adrenoceptor, vasopressin/arginine receptor, V1a, prostaglandin F2 alpha receptor, growth hormone secretagogue receptor 1 (GHSR), cholecystokinin receptor, NMDAR2A N-METHYL-D-ASPARTATE RECEPTOR SUBUNIT, P2U PURINOCEPTOR 1 (ATP RECEPTOR) (P2U1) PURINERGIC RECEPTOR), estrogen receptor beta (ER-beta), ESR2, NR3A2, kappa-type opioid receptor (KOR-I), lutropin-choriogonadotropic hormone receptor, beta 1 adrenergic receptor (ADRB1R), 5-hydroxytryptamine (serotonin) receptor 1B, 5-HT1B, adrenergic receptor, beta 2, muscarinic acetylcholine receptor M3 (MACHR), B1 bradykinin receptor, mu opioid receptor (MUOR1), mu-type opioid receptor (MOR-I), opioid receptor B, serotonin 5HT2 receptor, somatostatin receptor 2, melatonin receptor, somatostatin receptor, galanin receptor 1, neuromedin B receptor, transmembrane receptor UNC5H1, pancreatic polypeptide receptor PP1, interleukin-2 QL-2), somatostatin, luteinizing hormone, alpha, mast cell protease 1 precursor (RMCP-I), secretory protein probasin (M-40), E-selectin precursor, endothelial leukocyte adhesion molecule 1 (ELAM-I), leukocyte-endothelial

cell adhesion molecule 2 (LECAM2), CD62E, Protein kinase C-binding protein betalS, RING-domain containing, kidney band 3 anion exchange protein, SLC4A1, AE1, L-selectin precursor, lymph node homing receptor, leukocyte adhesion molecule-1 (LAM-1), LY-22, lymphocyte surface MEL-14 antigen, leukocyte-endothelial cell adhesion molecule 1 (LECAM1), CD62L, Wilms1 tumor protein (WT1), tumor suppressor, CD28, T-cell surface antigen, c-fgr proto-oncogene , CD3, gamma chain, cathepsin E, S-myc proto-oncogene protein, myc-related , G protein-activated inward rectifier potassium channel 4 (GIRK4), inward rectifier potassium channel subfamily J member 5 (KCNJ5), heart KATP channel, KATP-I, cardiac inward rectifier (CIR), KIR3.4, fructose (glucose) transporter, sodium channel protein 6 (SCP6), sodium channel, beta 1 subunit, sodium-hydrogen exchange protein-isoform 2 (NHE-2), PMCA, ATP2B2, calcium-transporting ATPase plasma membrane (brain isoform 2, EC 3.6.1.38), calcium pump, ATPase, sodium/potassium, gamma subunit, G protein-activated inward rectifier potassium channel 1 (GIRK1), inward rectifier potassium channel subfamily J member 3 (KCNJ3), KGA, KGB1, KIR3.1, proton gated cation channel drasic, sensory neuron specific, sodium channel 2, brain ATPase, copper-transporting, Menkes protein, channel-inducing factor precursor (CHIF), corticosteroid-induced protein, synaptotagmin II, carbonic anhydrase 4, calcitonin receptor precursor (CT-R), C1A/C1B, vasopressin V2 receptor, 5-hydroxytryptamine (serotonin) receptor IB, 5-HT1B, gamma-aminobutyric acid receptor alpha 4 subunit precursor (GABA(A) receptor, GABRA4), vitamin D3 receptor (VDR), 1,25-dihydroxyvitamin D-3 receptor, NR1I1, muscarinic acetylcholine receptor M5 (CHRM5), somatostatin receptor, galanin receptor 1, **granulocyte-macrophage colony-stimulating factor** (GM-CSF), colony- stimulating factor (CSF), guanylyl cyclase (membrane form), parathyroid hormone receptor PTH2, galanin receptor 2, 5- hydroxytryptamine (serotonin) receptor 2B, guanine nucleotide-binding protein G(I)/G(S)/G(O) gamma-7 subunit (GNG7, GNGT7), adenylyl cyclase 4, protein kinase C-binding protein nel homolog 1, phospholipase C beta 3 (PLC-beta 3), tissue-type plasminogen activator (t-PA), NW, neural visinin-like Ca2+-binding protein, VISININ-LIKE PROTEIN 1 (VOM) (NEURAL VISMM-LIKE PROTEIN 1) (NVL-I) (NVP-I) (21KD CABP), T-cell receptor CD3 zeta subunit, P-selectin precursor, granule membrane protein 140 (GMP-140), PADGEM, CD62P, leukocyte-endothelial cell adhesion molecule 3 (LECAM3), T-cell receptor gamma subunit, kidney band 3 anion exchange protein, SLC4A1, AE1, L-selectin precursor, lymph node homing receptor, leukocyte adhesion molecule-1 (LAM-1), LY-22, lymphocyte surface MEL-14 antigen, leukocyte-endothelial cell adhesion molecule 1 (LECAM1), CD62L, myelin PO protein precursor, MPZ, MAL, T-lymphocyte maturation-associated protein, myelin protein MVP17, ErbB3 EGF receptor-related proto-oncogene, HER3, CD 3OL receptor, lymphocyte activation antigen CD30, Ki-I antigen, CD30 precursor, zinc transporter (ZnT-I), CCHB3, calcium channel (voltage-gated), DIHYDROPYRIDINB-SENSITIVE L-TYPE, CALCIUM CHANNEL BETA-3 SUBUNIT, water channel aquaporin 3 (AQP3), 3-methylcholanthrene-inducible cytochrome P450 (P450MC), cytochrome P450 IA1 (CYPIA1), sodium/potassium-transporting ATPase beta 1 subunit (ATP1B1), glucose transporter 3,

ATP-sensitive inward rectifier potassium subfamily J member 8 (KCNJ8), UKATP-I, ATP-sensitive inwardly rectifying K+ channel KIR6.1, RJM, Rab3 effector in synaptic-vesicle **fusion**, neuronal acetylcholine receptor protein alpha-3 chain precursor, purmergic receptor P2X5, ligand-gated ion channel, sodium channel I, renal organic anion transporter (ROAT1) H- multispecific organic anion transporter (OAT1), neuronal acetylcholine receptor protein alpha 6 subunit precursor (CHRNA6, ACRA6), sodium channel, beta 1 subunit, sodium-hydrogen exchange protein-isoform 2 (NHE-2), PMCA, ATP2B2, calcium-transporting ATPase plasma membrane (brain isoform 2, EC 3.6.1.38), calcium pump, fibrinogen beta subunit (FGB), sulfonylurea receptor (SUR), glycine receptor alpha 3 subunit precursor (GLRA3), multidrug resistance protein 2 (MDR2), P-glycoprotein (PGY2), potassium channel, voltage gated, KV3.4, RAW3, KCNC4, sodium/chloride co-transporter, thiazide sensitive, synaptosomal associated protein 25, SNAP-25, SNAP, SNAP25, SUP, calcitonin receptor precursor (CT-R), C1A/C1B, gamma-aminobutyric acid (GABA-A) receptor, beta 1 subunit, NEUREXINI-BETA PRECURSOR, Non-processed neurexin I-beta Synaptic cell surface proteins + NEUREXIN I-ALPHA PRECURSOR, Non-processed neurexin I-alpha Synaptic cell surface proteins, alpha 2B adrenergic receptor (ADRA2B), alpha 2B adrenoceptor, neuropeptide Y receptor type 1, prostaglandin E2 receptor EP4 subtype, alpha 2C adrenergic receptor (ADRA2C), alpha 2C adrenoceptor, c-ErbA oncogene, thyroid hormone receptor alpha-1 (THRA1), gamma-aminobutyric acid receptor alpha 1 subunit precursor (GABA(A) receptor, (GABRA2), P2Y PURINOCEPTOR 6 (P2Y6), glutamate receptor 1 precursor (GIuR-I), GIuR-A, GIuR-K1, gamma-aminobutyric acid receptor alpha 3 subunit precursor (GABA(A) receptor, GABRA3), NMDAR2A N-METHYL-D-ASPARTATE RECEPTOR SUBUNIT, P2U PURMOCEPTOR 1 (ATP RECEPTOR) (P2U1) (PURMBRGIC RECEPTOR), 5-hydroxytryptamine (serotonin) receptor IB, 5-HTIB, glycine receptor, alpha 2A subunit, inhibitory, parathyroid hormone receptor PTH2, 5-hydroxytryptamine 5A receptor (5HT5A, HTR5A), serotonin receptor, REC17, acetylcholine receptor alpha, brain natriuretic peptide (BNP), 5-kDa cardiac natriuretic peptide, ISO-ANP, luteinizing hormone, alpha, cocaine/amphetamine-induced rat transcript, CART, protein kinase C-binding protein nel homolog 1, 14-3-3 protein eta, PKC inhibitor protein-1, KCIP-I, plectin, NVP, neural visinin-like Ca2+-binding protein, VISININ-LIKE PROTEIN 1 (VILIP-I) (NEURAL VISININ-LIKE PROTEIN 1) (NVL-I) (NVP-I) (21 KD CABP), **syndecan** 3, ras-GTPase-activating protein (GAP), ras p21 protein activator, p20GAP, interleukin-6 receptor beta chain, membrane glycoprotein gp1SO, prostatic secretory protein probasin (M-40), A-raf proto-oncogene, prothymosin-alpha (PTMA), cadherin 6 precursor, kidney-cadherin (K-cadherin), neurofibromin, neurofibromatosis protein type I (NF1), GTPase stimulatory protein, c-H-ras proto-oncogene, transforming G-protein p21, HSP84, HSP90-beta, heat shock 9OkD protein, Neural adhesion molecule F3, RAT NEURAL ADHESION MOLECULE F3, COMPLETE CDS, BIG-1 PROTEIN PRECURSOR, neural cell adhesion protein, neurite outgrowth-promotor, potassium channel protein, KSHIHA3, ATP-sensitive inward rectifier potassium channel subfamily J member 1 (KCNJ1), KAB-I, KIR1. 1, ROMK1, Band 3 (B3RP3), 3 Cl-HCO3-anion exchanger, voltage-gated potassium channel protein KV1. 1, RBK1, RCK1, KCNA1, potassium channel,

inward rectifier 9, taurine transporter, neuronal acetylcholine receptor protein alpha-3 chain precursor, sodium channel I, potassium channel protein CDRK, neuronal acetylcholine receptor protein alpha 6 subunit precursor (CHRNA6, ACRA6), calcium channel, alpha 1 beta, sodium channel, beta 1 subunit, PMCA, ATP2B2, calcium-transporting ATPase plasma membrane (brain isoform 2, EC 3.6.1.38), calcium pump, 17-kDa ubiquitin-conjugating enzyme E2 (UBE2B), ubiquitin-protein ligase, ubiquitin carrier protein, HR6B, synaptosomal associated protein 25, SNAP-25, SNAP, SNAP25, SUP, 67-kDa glutamic acid decarboxylase (GAD67), GAD1, eek proto-oncogene, protein tyrosine kinase, eph/elk-related, D(IA) DOPAMINE RECEPTOR, growth hormone receptor precursor (GH receptor, GHR), serum-binding protein, NMDAR2A N-METHYL-D-ASPARTATE RECEPTOR SUBUNIT, 5-hydroxytryptamine (serotonin) receptor IB, 5-HT1B, thyroid hormone beta receptor, c-erbA-beta, gamma-aminobutyric acid (GABA-A) receptor, beta 3 subunit, glutamate receptor 2 precursor (GLUR-2, GLUR-B, GLUR-K2), glutamate receptor 4 precursor (GLUR-4, GLUR-D), cannabinoid receptor 1, neuronal, neuromedin K receptor (NKR), neurokinin B receptor, NK-3 receptor (NK-3R), GABA-A receptor gamma-2 subunit precursor, galanin receptor 2, insulin-like **growth factor** binding protein 1 precursor (IGFBP-I, IBP-I), pre-somatotropin, protein kinase C beta-I type (PKC-beta I) + protein kinase C beta-II type (PKC-beta D), guanine nucleotide-binding protein G(O) alpha subunit (GNAO, GNAO), guanine nucleotide-binding protein G(I) alpha 1 subunit (GNAI1), adenylate cyclase-inhibiting G alpha protein, serine/threonine kinase PCTAIRE2 (PCTK2), protein kinase C-binding protein nel homolog 1, PKI-alpha, cAMP-dependent protein kinase inhibitor (muscle/brain form), 14-3-3 protein eta, PKC inhibitor protein-1, KCIP-I, and NW, or neural visinin-like Ca2+-binding protein, VISIN1N-LIKE PROTEIN 1 (VILIP-I) (NEURALVISININ-LIKE PROTEIN 1) (NVL-I) (NVP-I) (21 KD CABP).

ACTIVITY - Ophthalmologic; Nootropic; Neuroprotective; Antidiabetic; Anticonvulsant; Vulnerary; Antiparkinsonian; Cytostatic. No biological data given.

MECHANISM OF ACTION - Gene-Therapy.

USE - The methods and compositions are useful for the diagnosis, prevention and/or treatment of diseases or conditions associated with neuronal cell death, such as optic nerve degeneration, Alzheimer's disease, diabetic retinopathy, Huntington's disease, spinal cord injury, Parkinson's disease, glaucoma, neuronal tumor and age-related macular degeneration (claimed).

ADMINISTRATION - Routes of administration of the pharmaceutical compositions include intramuscular, intraperitoneal, intravenous, subcutaneous, intrarectal, transdermal and intranasal. No dosages given.

EXAMPLE - No relevant example given.(122 pages)

CLASSIFICATION: THERAPEUTICS, Protein Therapeutics; GENETIC TECHNIQUES and APPLICATIONS, Gene Expression Techniques and Analysis; DISEASE, Cancer; DISEASE, Central Nervous System; DISEASE, Endocrine/Metabolic System; DIAGNOSTICS, Molecular Diagnostics; THERAPEUTICS, Gene Therapy

CONTROLLED TERMS: RECOMBINANT NEURONAL MARKER PROTEIN PREP., ISOL., VECTOR-MEDIATED GENE TRANSFER, EXPRESSION IN HOST CELL, APPL. NEURODEGENERATIVE DISORDER, CANCER, DIABETES, GLAUCOMA

DIAGNOSIS, PREVENTION, THERAPY, GENE THERAPY TUMOR 6P21.3 (23, 16)

L64 ANSWER 31 OF 33 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
DUPLICATE 4
ACCESSION NUMBER: 2004-06797 BIOTECHDS
TITLE: New molecule comprising an antibody variable region that specifically binds to an extracellular domain of a tumor endothelium markers (TEM) protein, useful for inhibiting tumor growth or for promoting wound healing;
for use in gene therapy
AUTHOR: ST CROIX B; KINZLER K W; VOGELSTEIN B
PATENT ASSIGNEE: UNIV JOHNS HOPKINS SCHOOL MEDICINE
PATENT INFO: WO 2004001004 31 Dec 2003
APPLICATION INFO: WO 2003-US19544 23 Jun 2003
PRIORITY INFO: US 2003-458959 1 Apr 2003; US 2002-390187 21 Jun 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-082487 [08]
ABSTRACT: DERWENT ABSTRACT:
NOVELTY - A new isolated molecule comprises an antibody variable region that specifically binds to an extracellular domain of a tumor endothelium markers (TEM) protein.

DETAILED DESCRIPTION - new isolated molecule comprises an antibody variable region that specifically binds to an extracellular domain of a tumor endothelium markers (TEM) protein comprising potassium inwardly-rectifying channel, subfamily J, member 8, vascular cell adhesion molecule 1, NADH:ubiquinone oxidoreductase MLRQ subunit homolog, hypothetical protein MGC5508, **syndecan** 2, hypothetical protein BC002942, uncharacterized hematopoietic, stem/progenitor cells protein MDS032, FAT tumor suppressor homolog 1, G protein-coupled receptor 4, amyloid beta precursor protein, TNF receptor superfamily, member 25, MHC class I A, degenerative spermatocyte homolog, lipid desaturase, matrix metalloproteinase 25, prostate stem cell antigen, melanoma cell, adhesion molecule, protocadherin beta 9, matrix, metalloproteinase 14, scotin, chemokine ligand 14, murine retrovirus integration site 1 homolog, integrin alpha 11, interferon, inducible protein, CLST 11240 protein, H factor (complement)-like, tweety homolog 2, transient receptor potential, cation channel, subfamily V, member 2, hypothetical protein PRO1855, sprouty homolog 4, accessory protein BAP31, integrin alpha V, gap junction protein, alpha 4, 37kDa, calsyntenin 1, solute carrier family 26 member 6, family with sequence similarity 3 member C, immunoglobulin heavy constant gamma 3, hephestin, cisplatin, resistance related protein CRR9p, hypothetical protein IMAGE3455200, Homo sapiens mRNA full length insert cDNA clone EUROIMAGE881791, hypothetical protein MGC15523, prostaglandin I2 receptor, CD164 antigen sialomucin, putative G-protein coupled receptor GPCR41, DKFZP566H073 protein, platelet-derived **growth factor** receptor, alpha polypeptide, NADH dehydrogenase 1 alpha subcomplex 1, 7.5kDa, CD151 antigen, platelet-derived **growth factor** receptor, beta polypeptide, KIAA0102 gene product, B7 homolog 3, solute carrier family 4, anion exchanger, member 2, endothelin receptor type B, defender against cell death 1, transmembrane prostate androgen induced RNA, Notch homolog 3, lymphotoxin beta chondroitin sulfate

proteoglycan 4, lipoma HMGIC **fusion** partner, hypothetical protein similar to ankyrin repeat-containing protein AKR1, SDR1 short-chain dehydrogenase/reductase 1, PCSK7 proprotein convertase subtilisin/kexin type 7, Homo sapiens mRNA, cDNA DKFZp686D0720, FAP fibroblast activation protein alpha, MCAM melanoma cell adhesion molecule, CRELD1 cysteine-rich with EGF-like domains 1 or hypothetical protein DKFZp761D0211. INDEPENDENT CLAIMS are also included for the following: (1) a method of inhibiting neoangiogenesis; (2) a method for inhibiting tumor growth in a subject bearing a tumor; (3) a method for identifying a ligand involved in endothelial cell regulation; (4) a method for identifying a ligand involved in endothelial cell regulation; (5) a method for identifying a ligand involved in endothelial cell regulation; (6) a soluble form of a human transmembrane protein lacking a transmembrane domain; (7) a method of identifying regions of neoangiogenesis in a patient; (8) a method of screening for neoangiogenesis in a patient; (9) a method for identifying candidate drugs for treating tumors or wounds; (10) a method for identifying endothelial cells; (11) a method for inducing an immune response to a TEM protein in a mammal; (12) a method for stimulating vascular proliferation.

BIOTECHNOLOGY - Preferred Molecule: The molecule is an intact antibody molecule, single chain variable region (ScFv), humanized antibody or human antibody. It is bound to a cytotoxic, therapeutic or detectable moiety or to an antitumor agent. Preferred Method: Inhibiting neoangiogenesis comprises administering to a subject the isolated molecule comprising an antibody variable region that specifically binds to an extracellular domain of a TEM protein. The subject bears a vascularized tumor, polycystic kidney disease, diabetic retinopathy, rheumatoid arthritis or psoriasis. Inhibiting neoangiogenesis in a patient comprises administering to the patient the soluble form of a human transmembrane protein. Inhibiting tumor growth in a subject bearing a tumor comprises administering to the subject the isolated molecule. Identifying a ligand involved in endothelial cell regulation comprises contacting an isolated and purified human transmembrane protein and determining the amount of binding of the molecule comprising an antibody variable region to the human transmembrane protein, where a test compound that diminishes the binding of the molecule comprising an antibody variable region to the human transmembrane protein is identified as a ligand involved in endothelial cell regulation. The method further comprises contacting the test compound with endothelial cells and determining if the test compound inhibits growth of the cells. The endothelial cells are in culture or in a mammal. Identifying a ligand involved in endothelial cell regulation comprises: (1) contacting a cell comprising a human transmembrane protein with a test compound and the molecule comprising an antibody variable region that specifically binds to an extracellular domain of the human transmembrane protein; (2) determining amount of binding of the molecule comprising an antibody variable region to the cell; and (3) identifying a test compound that diminishes amount of binding of the molecule comprising an antibody variable region to the cell as a ligand involved in endothelial cell regulation. The method further comprises determining if the test compound

inhibits endothelial cell growth. The method also comprises: (1) contacting a test compound with a human transmembrane protein; (2) determining the binding of the test compound with the human transmembrane protein; and (3) identifying a test compound that binds to the protein as a ligand involved in endothelial cell regulation. The method further comprises testing the compound to determine whether it inhibits endothelial cell growth in culture or in a mammal. Identifying regions of neoangiogenesis in a patient comprises administering to the patient the isolated molecule comprising an antibody variable region that specifically binds to an extracellular domain of a protein and detecting the molecule bound to the detectable moiety in the patient. Screening for neoangiogenesis in a patient comprises contacting a body fluid collected from a patient with the molecule comprising an antibody variable region that specifically binds to an extracellular domain of a protein and detecting material in the body fluid that is cross-reactive with the molecule. Identifying candidate drugs for treating tumors or wounds comprises: (1) contacting a test compound with cells that express one or more genes comprising potassium inwardly-rectifying channel, subfamily J, member 8; (2) determining the amount of expression of the one or more genes by hybridization of mRNA of the cells or cDNA or cRNA copied from the mRNA to a nucleic acid probe that is complementary to an mRNA of the one or more genes; and (3) identifying a test compound as a candidate drug for treating tumors if it decreases expression of the one or more genes, or identifying a test compound as a candidate drug for promoting wound healing if it increases expression of the one or more genes. The cells are recombinant host cells that are transfected with an expression construct for expression of the one or more genes. The method also comprises: (1) contacting a test compound with cells that express one or more proteins comprising potassium inwardly-rectifying channel, subfamily J, member 8; (2) determining the amount of one or more proteins in the cells; and (3) identifying a test compound as a candidate drug for treating tumors if it decreases the amount of one or more proteins in the cells, or identifying a test compound as a candidate drug for promoting wound healing if it increases the amount of one or more proteins in the cells. The method also comprises: (1) contacting a test compound with cells that express one or more proteins comprising potassium inwardly-rectifying channel, subfamily J, member 8; (2) determining the activity of one or more proteins in the cells; and (3) identifying a test compound as a candidate drug for treating tumors if it decreases the activity of one or more proteins in the cells, or identifying a test compound as a candidate drug for promoting wound healing if it increases the activity of one or more proteins in the cells. Identifying endothelial cells comprises: (1) contacting a population of cells with one or more molecules comprising a variable region that binds specifically to the protein; (2) detecting cells in the population that have bound to the molecules; and (3) identifying cells that are bound to the one or more molecules as endothelial cells. The method further comprises isolating cells that have bound to the one or more molecules from cells that have not bound. The one or more molecules are intact antibodies. The method also comprises: (1) contacting cDNA or mRNA of a population of

cells with one or more nucleic acid hybridization probes that are complementary to a cDNA or mRNA for the gene; (2) detecting cDNA or mRNA that have specifically hybridized to the nucleic acid hybridization probes; and (3) identifying cells whose nucleic acids specifically hybridized to the nucleic acid hybridization probes as endothelial cells. Inducing an immune response to a TEM protein in a mammal comprises administering to a human subject who has or is at risk of developing a tumor a TEM protein or nucleic acid encoding a TEM protein and administering an immune adjuvant. Stimulating vascular proliferation comprises administering to a subject with a wound the TEM protein or nucleic acid encoding TEM protein, where wound healing is promoted.

ACTIVITY - Vulnerary; Cytostatic. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The molecule is useful for inhibiting tumor growth, for inducing an immune response to a TEM protein or for stimulating vascular proliferation for promoting wound healing (claimed).

EXAMPLE - No relevant examples given. (107 pages)

CLASSIFICATION: THERAPEUTICS, Protein Therapeutics; GENETIC TECHNIQUES and APPLICATIONS, Gene Expression Techniques and Analysis; DISEASE, Cancer; THERAPEUTICS, Gene Therapy

CONTROLLED TERMS: RECOMBINANT TUMOR ENDOTHELIUM MARKER PROTEIN PREP., ISOL., VECTOR-MEDIATED GENE TRANSFER, EXPRESSION IN HOST CELL, APPL. VULNERARY, CANCER THERAPY, GENE THERAPY TUMOR (23, 13)

L64 ANSWER 32 OF 33 BIOTECHDS COPYRIGHT 2005 THE THOMSON CORP. on STN
DUPLICATE 5

ACCESSION NUMBER: 2003-16828 BIOTECHDS

TITLE: Comparison of gene expression profile in tissue sample with known profiles of normal and pathological tissue for determination of presence and progression stage of multiple myeloma;
expression profiling useful for cancer diagnosis and prognosis

AUTHOR: MANO H

PATENT ASSIGNEE: FUJISAWA PHARM CO LTD

PATENT INFO: WO 2003038088 8 May 2003

APPLICATION INFO: WO 2002-JP11257 30 Oct 2002

PRIORITY INFO: JP 2001-337752 2 Nov 2001; JP 2001-337752 2 Nov 2001

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

OTHER SOURCE: WPI: 2003-430523 [40]

ABSTRACT: DERWENT ABSTRACT:
NOVELTY - Investigation (M1) of multiple myeloma in which the expression level of genes associated with multiple myeloma in an investigative sample is compared with that in normal tissue or in MGUS (monoclonal gammopathy of undetermined significance), MM (multiple myeloma) or PCL (plasma cell leukemia) stage multiple myeloma tissue, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) screening (M2) compounds for the treatment and prevention of multiple myeloma, in which the expression level and profile of the multiple myeloma-associated genes in test animals or test cells is compared in the presence or absence of the test compound, or the activity of the expression products of one or more of the genes is compared in the presence or absence of the test compound; (2)

compounds identified by M2; (3) treatment and prevention (M3) of multiple myeloma using antisense nucleic acids to mRNA for one or more of the multiple myeloma-associated genes; (4) treatment and prevention (M4) of multiple myeloma using ribozymes cleaving mRNA for one or more of the multiple myeloma-associated genes; (5) treatment and prevention (M5) of multiple myeloma using antibodies to the expression products of one or more of the multiple myeloma-associated genes; (6) risk determination (M6) of multiple myeloma development by determining the expression profile of the multiple myeloma-associated genes or the activity of their expression products; (7) detection (M7) of multiple myeloma cells using M1.

BIOTECHNOLOGY - Preferred Method: The genes compared in M1 include one or more of WEE1, HVEM, histone H2A, LD78alpha, GIPR, CTGF, cytochrome b alpha-subunit, MHC homologues, THBP, CRHP, liposome protein L28, **growth factor** receptor, immunoglobulin Ig lambda-chain, laminin receptor, liposome protein L18, NM23-H1, 28kDa heat-shock protein, immunoglobulin transcript 3 protein variant 1, GsGTP binding protein alpha-subunit, M9, macrophage motility inhibitory factor, K1AA1042 protein, APR peptide, RING6, human H-factor homologues and KIAA0832 protein genes. The investigative sample is a sample of **CD138**-positive bone marrow cells. The expression level of the multiple myeloma-associated genes is measured by mRNA assay (by gene amplification, DNA chip analysis, DNA microassay analysis or northern blotting) or by assay of the gene expression products (by immunochemical assay or protein chip analysis). Test animals or test cells used for screening compounds for the treatment and prevention of multiple myeloma may be transformed with a gene or genes encoding **fusion** proteins of the multiple myeloma-associated gene products with a reporter protein; the expression level of the reporter is then measured in the presence or absence of the test compound.

USE - M1 is useful for the determination of the existence or stage of progression of multiple myeloma and the risk of its development, and screening substances for their ability to treat or prevent multiple myeloma.

EXAMPLE - Bone marrow samples are taken from normal subjects and from patients at various stages of the progression of multiple myeloma. Monocytes are isolated from the bone marrow samples and **CD138**+ cells separated using anti-**CD138**+ MicroBeads (Milteny Biotech). Total RNA is isolated from these **CD138**+ cells, biotin-labelled and hybridised to a GeneChip HGU95Avs2 microarray (Affymetrix) (12625 genes). Expression levels are evaluated using GeneSpring 4.1.1 software (Silicon Genetics). Significant differences in expression in normal and pathological tissue are found for 28 genes. For example, LD78alpha gene (GenBank D90144) has a mean relative expression level of 2.1 in normal tissue, 4.3 in MGUS tissue, 31.1 in MM tissue and 27.8 in PCL tissue. (128 pages)

CLASSIFICATION: GENETIC TECHNIQUES and APPLICATIONS, Gene Expression Techniques and Analysis; BIOINFORMATICS and ANALYSIS, Biochips and Bioarrays; DISEASE, Cancer; DIAGNOSTICS, Molecular Diagnostics

CONTROLLED TERMS: WEE1, HVEM, HISTONE-H2A, LD78-ALPHA, GIPR, CTGF, CYTOCHROME-B-ALPHA-SUBUNIT, MAJOR HISTOCOMPATIBILITY COMPLEX,

THBP, CRHP, LIPOSOME PROTEIN-L28, GROWTH FACTOR RECEPTOR, IMMUNOGLOBULIN, LAMININ RECEPTOR, LIPOSOME PROTEIN-L18, NM23-H1, HEAT SHOCK PROTEIN-28, GSGTP BINDING PROTEIN ALPHA-SUBUNIT, M9, MACROPHAGE MOTILITY INHIBITORY FACTOR, K1AA1042 PROTEIN, APR PEPTIDE, RING6, HUMAN H-FACTOR, KIAA0832 PROTEIN, MULTIPLE MYELOMA-ASSOCIATED GENE EXPRESSION PROFILING, DNA AMPLIFICATION, DNA CHIP, DNA MICROARRAY, NORTHERN BLOT HYBRIDIZATION ANALYSIS, DRUG SCREENING, APPL. MUTLIPLE MYELOMA, PLASMA CELL LEUKEMIA DIAGNOSIS, PROGNOSIS BIOCHIP DNA ARRAY BIOARRAY CANCER TUMOR (22, 28)

L64 ANSWER 33 OF 33 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-162980 [17] WPIDS
DOC. NO. CPI: C2005-052696
TITLE: Novel anti-CD19 monoclonal antibody that binds CD19 antigen, useful for treating B-cell disease such as lymphoma, leukemia, or autoimmune disease such as myasthenia gravis, lupus nephritis, rheumatic fever, diabetes mellitus.
DERWENT CLASS: B04 D16 K08
INVENTOR(S): GOLDENBERG, D M; HANSEN, H J; QU, Z
PATENT ASSIGNEE(S): (IMMU-N) IMMUNOMEDICS INC
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005012493	A2	20050210	(200517)*	EN	81	C12N000-00

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005012493	A2	WO 2004-US24636	20040802

PRIORITY APPLN. INFO: US 2003-491282P 20030731
INT. PATENT CLASSIF.:
MAIN: C12N000-00
BASIC ABSTRACT:
WO2005012493 A UPAB: 20050311
NOVELTY - A monoclonal antibody or its fragment (I) that binds a CD19 antigen, where (I) is chimeric, humanized or is fully human, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an antibody fusion protein or its fragment (II), comprising at least two MAbs or their fragments, where each of the MAbs independently is an anti-CD19 MAb of (I), or (I) and a second MAb or its fragment, where the second MAb or its fragment is other than (I);
(2) a nucleic acid (III) comprising a sequence encoding (I) or (II);
(3) an expression vector (IV) comprising (III);
(4) a host cell (V) comprising (III); and
(5) a B-cell targeting diagnostic or therapeutic conjugate (VI),

comprising an antibody component bound to at least one diagnostic or at least one therapeutic agent, where the antibody component comprises (I) or (II).

ACTIVITY - Cytostatic; Immunosuppressive; Hemostatic; Muscular-Gen,; Neuroprotective; Antiinflammatory; Dermatological; Antirheumatic; Antidiabetic; Antiulcer; Gastrointestinal-Gen.; Antiarthritic; Anabolic; Hypertensive; Nephrotropic; Thyromimetic; Hepatotropic; Antiallergic; Vasotropic; Antianemic; Antipsoriatic; Endocrine-Gen. No supporting data is given.

MECHANISM OF ACTION - Evocates humoral and/or cellular immune response.

USE - (I) is useful for treating B-cell disease in a subject, which involves administering (I) formulated in a pharmaceutically acceptable vehicle. The B-cell disease is lymphoma, leukemia, or autoimmune disease such as acute idiopathic thrombocytopenic purpura, chronic idiopathic thrombocytopenic purpura, dermatomyositis, Sydenham's chorea, myasthenia gravis, systemic lupus erythematosus, lupus nephritis, rheumatic fever, polyglandular syndromes, bullous pemphigoid, diabetes mellitus, Henoch-Schonlein purpura, post-streptococcalnephritis, erythema nodosum, Takayasu's arteritis, Addison's disease, rheumatoid arthritis, multiple sclerosis, sarcoidosis, ulcerative colitis, erythemia multiforme, IgA nephropathy, polyarteritis nodosa, ankylosing spondylitis, Goodpasture's syndrome, thromboangitisubiterans, Sjogern's syndrome, primary biliary cirrhosis, Hashimoto's thyroiditis, thyrotoxicosis, scleroderma, chronic active hepatitis, polymyositis/dermatomyositis, polychondritis, pamphigus vulgaris, Wegener's granulomatosis, membranous nephropathy, amyotrophic lateral sclerosis, tabes dorsalis, giant cell arteritis/polymyalgia, pernicious anemia, rapidly progressive glomerulonephritis, psoriasis and fibrosing alveolitis. The method further involves administering to the subject concurrently or sequentially a therapeutically effective amount of humanized, **chimeric**, human or murine MAb chosen from MAb reactive with CD4, CD5, CD8, CD14, CD15, CD19, CD20, CD21, CD22, CD23, CD25, CD33, CD37, CD38, CD40, CD40L, CD46, CD52, CD54, CD74, CD80, CD126, **CD138**, B7, MUC1, Ia, HM1.24, HLA-DR, tenascin, vascular endothelial **growth factor** (VEGF), PIGF, ED-B fibronectin, oncogene, oncogene product, NCA 66a-d, necrosis antigens, Ii, interleukin (IL)-2, T101, TAC, IL-6, tumor necrosis factor-related apoptosis-inducing ligand (TRAIL)-R1 (DR4) and TRAIL-R2 (DR5), formulated in a vehicle. The method further involves administering to the subject concurrently or sequentially therapeutic agent, formulated in a pharmaceutically acceptable vehicle, or a therapeutic conjugate comprising at least one MAb bound to at least one therapeutic agent. (I), (II) and (VI) are useful for treating B-cell disease or syndrome in a subject. The subject is a mammal. The mammal is a human dog or cat. (II) is useful for diagnosing or treating B-cell disease in a subject, which involves administering (II) formulated in a pharmaceutically acceptable vehicle, optionally a clearing agent and targetable conjugate reactive with (II). (IV) is useful for expressing (I) or (II), which involves transfecting a mammalian cell with (IV), and culturing the transfected cell. (VI) is useful for diagnosing a B-cell disease in a subject (all claimed).

Dwg.0/6

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B04-C01; B04-E03A; B04-E08; B04-F02A0E; B04-G01; B04-G05; B04-G21; B04-H01; B04-L01; B04-N04; B04-N04A; B04-N04B; B04-N06; B04-N08; B05-A01B; B05-A03A; B05-A03A1; B05-A03A2; B05-A03B; B05-A04; B05-B02A3; B05-C05; B05-C06; B05-C07; B05-C08; B10-C02; B11-C07A3; B11-C07A4; B12-K04A; B12-M11F; B14-A02; B14-C03; B14-C04; B14-C06; B14-C08;

B14-C09; B14-D01; B14-E10C1; B14-F03; B14-F08;
B14-G02; B14-H01A; B14-H01J; B14-J01; B14-J05;
B14-K01; B14-N10; B14-N11; B14-N12; B14-N16;
B14-N17; B14-S01; B14-S04; B14-S16; D05-H09;
D05-H11A2; D05-H12A; D05-H12E; D05-H14B2; D05-H17C1;
K08-X; K09-B01

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